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**13. ABSTRACT (Maximum 200 Words)**
In the first year of this study, we have developed gene therapy approaches for fracture repair by: 1) identifying regulatory sequences providing maximum transgene expression by two gene therapy vectors in the bone cells that mediate fracture repair; 2) developing vector delivery techniques for optimal therapeutic gene expression in the healing fracture; and 3) identifying therapeutic gene candidates to augment and accelerate fracture repair. Maximum transgene expression in primary and transformed bone cells was obtained using the non-specific murine leukemia (MLV)-based long terminal repeat and the lentiviral cytomegalovirus promoters, and the gene-specific elongation factor 1a promoter with the lentiviral-based vector. Using the MLV-based vector, surgical techniques have been developed to deliver gene therapy to the fracture site and optimize transgene expression for optimal therapeutic effect. These techniques have benefited healing by augmenting BMP-4 mediated bone formation in the fracture gap. The healing fracture tissues of four individual subjects have been examined for gene expression by microarray analysis at both 3 days and 11 days healing to identify therapeutic gene candidates. Several hundred genes and expressed sequence tags displayed statistically significant changes in expression at each time. Several candidates are currently undergoing confirmation of expression and further functional characterization.

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## INTRODUCTION

Battlefield injuries to the musculoskeletal system optimally require rapid wound healing and occasionally regeneration of the wounded tissues. Gene therapy has great potential to help rapidly heal such battlefield injuries, including soft-tissue as well as hard-tissue injuries. Fracture repair requires a complex series of molecular events that coordinate the proliferation and differentiation of diverse periosteal tissues that bridge the injury with bone that is identical to native bone and lacks scar tissue (Bolander, 1992). Different families of growth factors have been implicated that mediate diverse pathways of cell chemotaxis and tissue proliferation and differentiation during fracture repair (Barnes et al., 1999; Beasley and Einhorn, 2000). To elucidate the molecular pathways that mediate repair of diverse fracture tissues, the expression of growth factors and their receptors during fracture repair must be characterized and the physiological and morphological effects following local or systemic administration of their genes must be tested. However, gene therapy technology is still in its infancy and scientists have only begun to develop systems that both deliver growth factor genes and regulate their expression in injured tissues to augment normal and impaired healing.

Currently, our gene therapy approach has the potential to regenerate large skeletal defects, certainly an advantage for the repair of battlefield injuries of the musculoskeletal system. In our studies, we are optimizing fracture gene therapy using the hybrid growth factor transgene, bone morphogenetic protein (BMP)-2/4, expressed from constitutively by a Murine leukemia (MLV)-based vector or in a gene-specific manner by a lentiviral-based vector. Surgical techniques have been developed to optimize the delivery of the viral vector of choice to the healing fracture in small animals. The combination of efficient vector expression with optimal surgical delivery to the fracture will maximize the therapeutic effect for study. However, we also anticipate that to truly optimize gene therapy for fracture healing, more than one therapeutic gene may be required. In light of this, we have undertaken microarray studies of the fracture callus of multiple individual animal subjects to understand both gene expression in the response to bone injury, as well as those molecular factors that might delay the healing of such injuries. Several hundred genes that exhibit changes in expression at two different healing times have been identified, and those with therapeutic potential will be considered for inclusion in study in our gene therapy system. We propose that the efficient delivery and expression of growth factor, receptor and corresponding signaling pathway genes will, when expressed with BMP-4, enhance fracture healing. Ultimately, the development of these approaches could not only enhance the broad-spectrum fracture repair, but genetic algorithms to predict the response of individual military personnel to battlefield injury could individualize their therapy.

Our goals for the first twelve months of the funding period for each of the Technical Objectives below, as well as progress to date for each technical objective, are described below. This progress report is organized according to the outline provided by the office of the US Army Medical research and Material Command.

In addition to completing all the Technical Objectives required for this report period, we are reporting progress on additional objectives accomplished above and beyond those contracted for. These additional objectives are identified in the report as they are pertinent.

**BODY**

1. TECHNICAL OBJECTIVE 1: TO OPTIMIZE A GENE THERAPY FOR FRACTURE HEALING

a) Specific Objective 1: To Optimize Gene Expression and Protein Production of Growth Factor genes from Periosteal Cells Transduced with MLV-based or Lentiviral-based Vectors

1) Objective

This goal of this study is to identify the optimum viral-based vector and regulatory (promoter) elements for fracture gene therapy by comparing transfection and expression frequencies of Murine Leukemia virus (MLV)-based and lentiviral-based gene therapy vectors and promoters in periosteal and endosteal cells.

2) Materials and Methods

Periosteal cells were aseptically isolated from the unfractured hindlimb bones of Sprague-Dawley rats. The femurs and tibias were removed at sacrifice, the epiphyses removed and the diaphyseal marrow ablated with saline. The diaphyses were digested once with 0.25% trypsin and twice with 0.20% collagenase II for 2 hours each. The digests separated the periosteal and endosteal cells from the cortical bone and yielded dispersed and heterogeneous populations of the fibroblastic and cambial cells. These adherent cells were retained in culture while nonadherent contaminating marrow cells were discarded. Cell preparations of periosteal and endosteal origins provided a representative population of cells to be targeted for viral transduction by external or internal injection techniques. These cells were cultured at a low passage number for the subsequent comparison of transgene expression from transfected MLV-based or the lentiviral-based vectors.

To obtain optimal estimates of the relative transgene expression efficiencies for the MLV-based and lentiviral-based vectors, the Enhanced Green Fluorescent Protein (EGFP) was used as the transgene. Vector efficiency was established by target cell EGFP expression, which was regulated by the long terminal repeat (LTR) promoter in the case of the MLV-based vector, or by one of five gene-specific promoters in the case of the lentiviral-based vector. These five gene-specific promoters were derived from the cytomegalovirus (CMV), elongation factor 1-alpha (EF-1a), collagen 1, collagen 2.3 and core-binding factor alpha-1 (cbfa-1) genes.

Each vector and promoter-EGFP combination was transduced into the periosteal and endosteal cell cultures in duplicate (n = 2). Additionally, the mouse osteoblast MC-3T3 cell line was assayed for EGFP expression as a known bone cell line. Because variable transgene expression from different promoters makes the virus difficult to titer, 10 ul and 50 ul volumes of each viral vector stock were compared for transfection and expression frequencies. The numbers of cells expressing EGFP were quantified by fluorescent cell sorting following 48 hours of culture.

3) Results

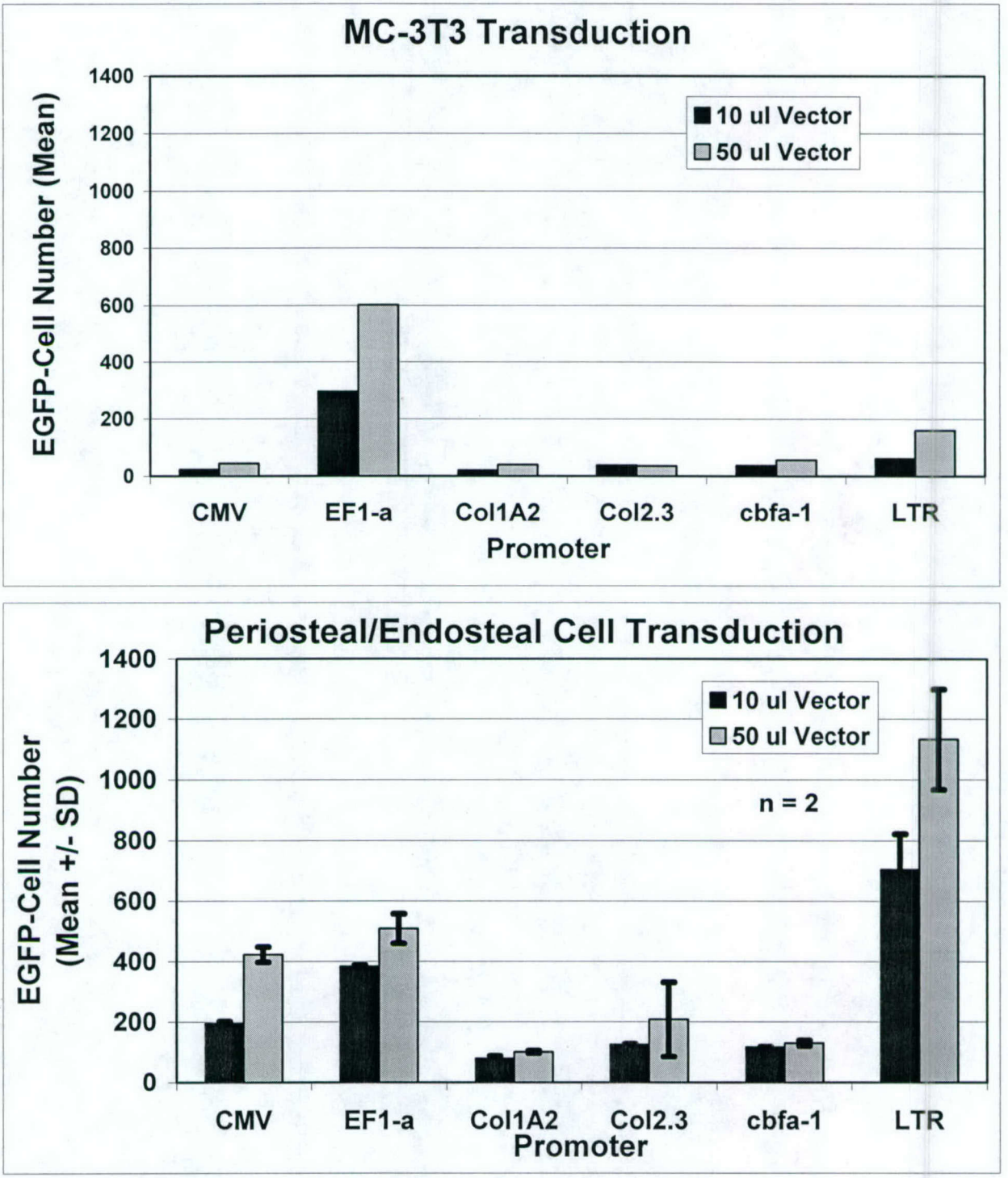



Figure 1. Mean EGFP expression in MC-3T3 (top) periosteal/endosteal bone cells (bottom) from the LTR promoter in an MLV vector, or other promoters (CMV, EF1-a, Col IA2, Col 2.3, cbfa-1) in a lentiviral-based vector.

As expected, the powerful LTR promoter of the MLV-based vector provided the greatest numbers of EGFP-expressing cells in the endosteal/periosteal cells (Figure 1). Among the lentiviral-based vector promoters, the EF-1a promoter provided the best expression at the 10 ul transfections, with more cells expressing the transgene than even the very robust CMV promoter. Surprisingly, the promoters derived from genes normally associated with bone cells, but most notably the collagen 2.3 and the cbfa-1 displayed much weaker transfection and expression frequencies. The results were consistent at both volumes of viral vectors transfected, although there was a more pronounced improvement in the MLV-based vector and the lentiviral-CMV promoter combination at the 50 ul volume than with the other lentiviral-based vector promoters. The lentiviral-EF1-a promoter results were also observed in the MC-3T3 cell line, suggesting that the results in the isolated periosteal and endosteal cells were indeed representative of bone cells. In this case the expression from this promoter was even greater than the MLV-LTR.

4) Conclusions

We conclude that either the MLV-based vector with the LTR promoter or the lentiviral-based vector with the EF-1a promoter provide the optimal transfection and expression of the transgene in the bone cells expected to modulate fracture healing. These vector and promoter combinations will be used for therapy when the optimal delivery technique (Specific Objective 2, below) and the therapeutic gene candidate(s) (Technical Objective 2, microarray analysis) are identified.

b) Specific Objective 2: To Compare the Local Periosteal Injection of the Virus at the Fracture Site with the Intramedullary Inoculation Procedure

1) Objective

Surgical techniques have been adapted to apply the viral-based vectors from either the exterior aspects of the rat femoral fracture callus or through the intramedullary space to the interior of the fracture callus. Multiple exterior injections and intramedullary injection techniques have been developed to maximize the symmetry localization of growth factor expression to the fracture site and compared for their ability to maximize the therapeutic benefit of the growth factor. We hypothesized that the medullary pressure injection would provide a more symmetric distribution of the therapy to the fracture.

2) Materials and Methods

*i) Fracture Surgery*

The fracture surgery for exterior injections is as previously described in the rat femur fracture model (Bonnerans and Einhorn, 1984). A stainless steel Kirschner wire (pin) is inserted into the femoral medullary canal to stabilize the fracture (Figure 2a), which is produced immediately after surgery by the three-point bending technique (Figure 2c). Post-fracture injections are performed from the exterior lateral or medial aspects of the leg. However, we have also adapted this surgery to aseptically insert a 20G catheter into the medullary canal of the femur alongside the stabilizing pin (Figure 2b, 2c). This catheter permits the post-fracture anterograde insertion of a needle into the medullary canal from the greater trochanter for the delivery of vectors expressing growth factor genes to the interior of the fracture at different times after the fracture.

*ii) Fracture Injection*

The therapeutic gene chosen was the BMP-2/4 hybrid gene and the B-galactosidase gene was chosen as the control (marker). Each was expressed from the MLV-based vector (Figure 3).

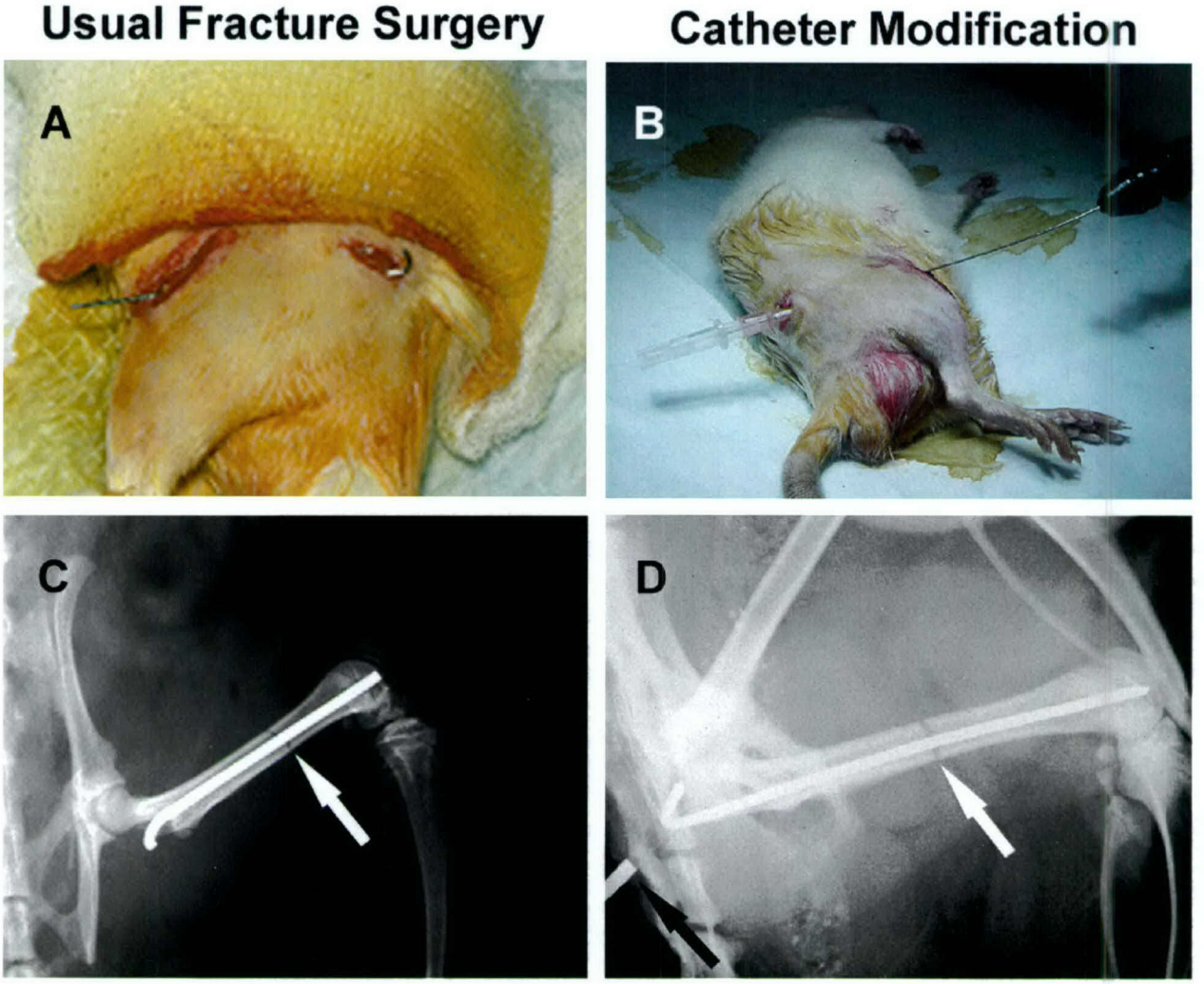



**Figure 2. The usual femur fracture surgery (left) and catheter modification (right).**
**A stabilizing Kirschner wire is inserted into the medullary space, hooked (A), seated at the greater trochanter and cut flush with the condyle prior to fracture (C, white arrow) by three-point bending.**
**In the catheter insertion modification, a 20 gauge catheter is inserted from the greater trochanter beside the wire inside the medullary space (B). The fracture is again produced by three-point the bending technique (D, white arrow). The external catheter hub is visible (D, black arrow), though the internal tubing cannot be visualized by X-Ray.**

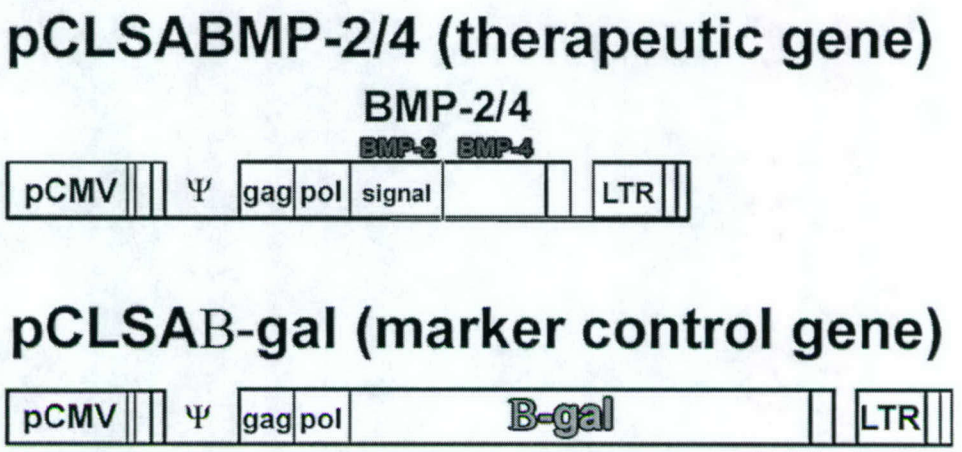



Figure 3. MLV gene constructs used for injection into the fracture.
The hybrid BMP-2/4 transgene (top) contains the human BMP-4 gene and BMP-2 signal sequence. The signal sequence was found to enhance BMP-4 secretion. The bacterial B-galactosidase gene has previously served both as a marker gene and as a non-therapeutic control gene for comparison with the BMP-2/4 gene. Expression for each gene is driven by the long terminal repeat (LTR) of the MLV-based vector.

We have previously used the fracture model for exterior injections of these genes to the lateral aspect of the femur (Figure 4a; Rundle et al., 2003). These injections attempt to deposit the therapy in the periosteal cambial layer on the cortical surface of the fractured femur. The accuracy of these injections was maximized using a fluoroscope to visualize the injection point relative to the fracture (Figure 4c). The fluoroscope was also used to monitor the accuracy of injections through the intramedullary catheter. The needle was easily inserted through the external opening of the catheter (Figure 4b), into the medullary space, and placed immediately proximal to the fracture for the injection (Figure 4d). In each case, 150 ul of vector was injected, a volume calculated to deliver between 15 million and 150 million viral particles at the titers produced by our Viral Vector Core Facility.

Because we have been testing these applications with the MLV-based vector, which requires proliferating tissue targets for transduction, we have injected the fracture tissues at one day post-fracture, when cell proliferation in the wound has started. However, because the lentiviral vector does not require actively proliferating cells for transduction, the post-fracture injection times can be altered to maximize the therapeutic benefit of a particular transgene.

3) Results

*i) Marker Localization in the Fracture Following Exterior or Intramedullary Injection*

Initially, we sought to localize fluids in the fracture by each injection method. To visualize the injection, 100 ul of a radio-opaque medical contrast dye was injected into the fracture site by either the lateral method or through the catheter. Its location was easily determined in real time using the fluoroscope. The injection of the contrast dye from the lateral aspect of the fracture was distributed in the muscle within the leg; very little appeared to penetrate the periosteum, where the target cells for fracture therapy reside (Figure 5a). The injection through the catheter was much more encouraging (Figure 5b). In this case, the contrast

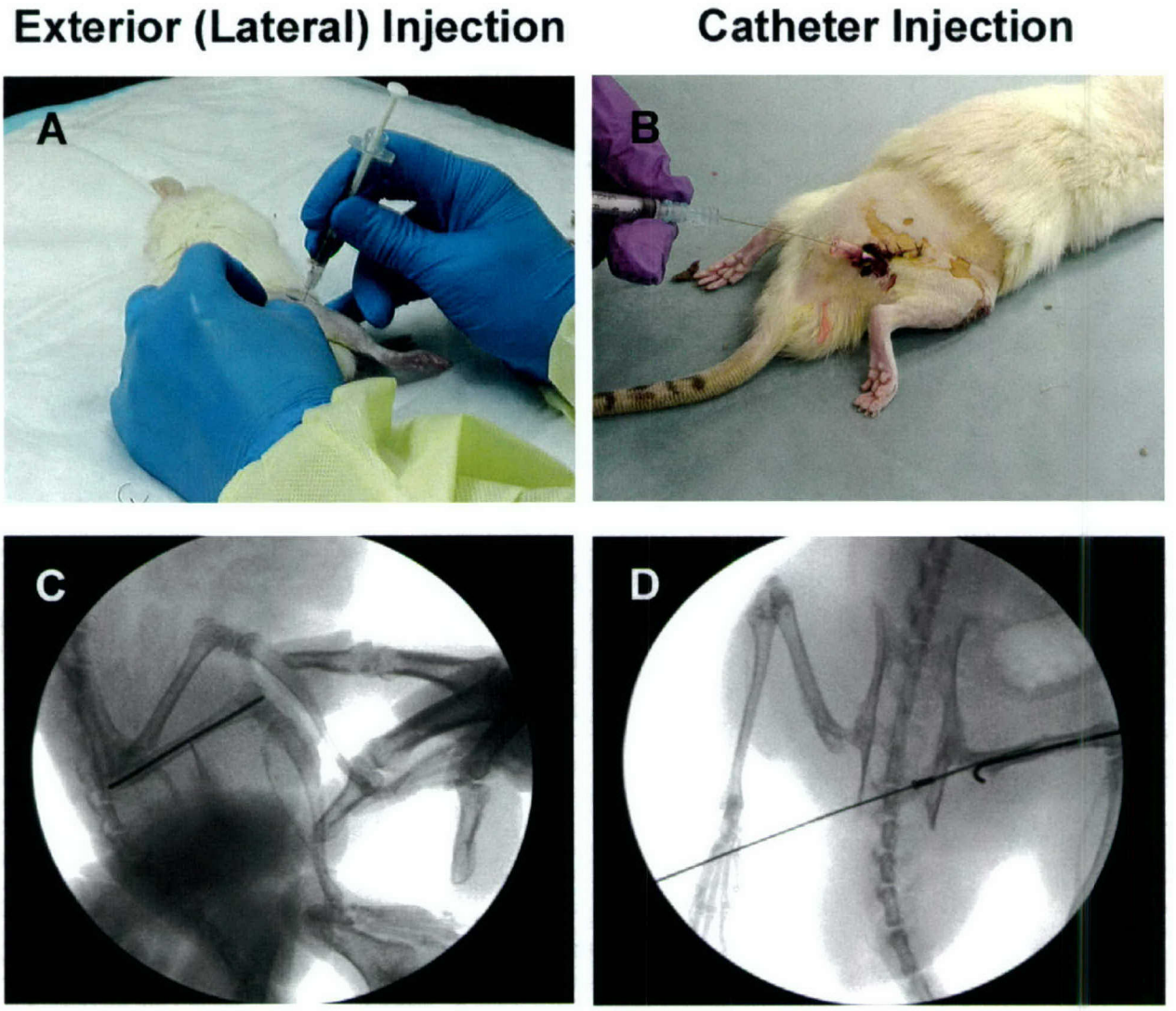



**Figure 4. Exterior (left) and interior (catheter, right) injection techniques. Injections from the exterior lateral aspect of the leg (A) used a fluoroscope to accurately place the needle at the fracture periosteum for injection (C). Catheter injections inserted a 25 gauge spinal needle through the catheter hub (B) into the femoral medullary space to deposit the injection at the fracture, again visualized using a fluoroscope (D).**

dye filled the medullary space and leaked out the wounds at the (proximal) greater trochanter and the (distal) condyle, where the pin was inserted. However, much of the dye also appeared to distribute to the fracture. Based upon these results the volume of the medullary canal was estimated to be approximately 150 ul, and the accuracy of transgene delivery and efficiency of transgene expression was examined.

To compare the accuracy of transgene delivery and expression between exterior lateral and the catheter injection techniques, 150 ul of MLV-based vector expressing a B-galactosidase marker gene was then applied at one day post-fracture. The animal was sacrificed at one week of healing and B-galactosidase gene expression was localized by splitting the bone and staining both the exterior (Figure 5c) and interior (Figure 5d) for B-galactosidase activity. When applied from the exterior lateral aspect of the fracture, marker gene transfection and expression was confined to a variable area at the periosteal surface that is certainly of limited efficacy for the distribution of any therapeutic gene to the fracture periosteal target cells (Figure 5c and d, top). This injection technique is inherently difficult during early healing; although it is the most clinically relevant time for therapy, the periosteal tissue layer is very thin, and presents a poor target. Consequently, most of the injection must have spilled into the surrounding muscle, as observed with the contrat dye injection. However, when applied from the interior of the fracture at one day using an intramedullary catheter, B-galactosidase marker gene expression after the same healing period was more symmetrically distributed around the fracture circumference, propagating throughout the periosteal tissues (Figure 5c and d, bottom). In accordance with MLV-based vector requirements for proliferating cells for transduction, B-galactosidase expression remained localized to the wounded and proliferating tissues at the fracture site. The therapy was concentrated at the fracture, either not being retained in the medullary canal or, if retained, lacking the proliferating target cells necessary for transduction. The catheter surgery technique therefore successfully avoided creating intramedullary injury and resident cell proliferation substantial enough for MLV-based vector transgene expression, and successfully confined transgene expression to the injured tissues of interest, namely the fracture. Moreover, as we have previously observed, the fractures that received B-galactosidase gene displayed normal callus size and content. Expression of this marker gene can therefore be used as a control for comparison with therapeutic gene expression. In summary, the catheter application technique will be much better for the even distribution of prospective therapeutic genes and for the determination of their therapeutic value during healing.

*ii) BMP-2/4 Gene Fracture Therapy Following Injection from the Exterior or Through the Intramedullary Catheter*

Exterior injections of MLV-based vector expressing the BMP-2/4 transgene, either from the lateral aspect or a combination of lateral and medial aspects were compared with injections to the intramedullary space through the surgically implanted catheter. The BMP-2/4 gene was chosen as the transgene to develop the therapeutic delivery because of its documented ability to efficiently differentiate osteogenic precursors to bone (Peng et al., 2001). As such, inaccurate delivery of the transgene can be easily established by the appearance of ectopic bone.

The therapy produced by each injection was monitored at 7, 14, 21 and 28 days healing via X-ray examination for mineralized tissues in live animals. Lateral injections always produced asymmetric bone formation (Figure 6a, c, e, g) that was obviously ectopic at 14 and 21 days healing (Figure 6c, e), when endochondral bone formation is at its peak. This condition was almost certainly produced by transgene expression in interstitial muscle cells of the fractured leg

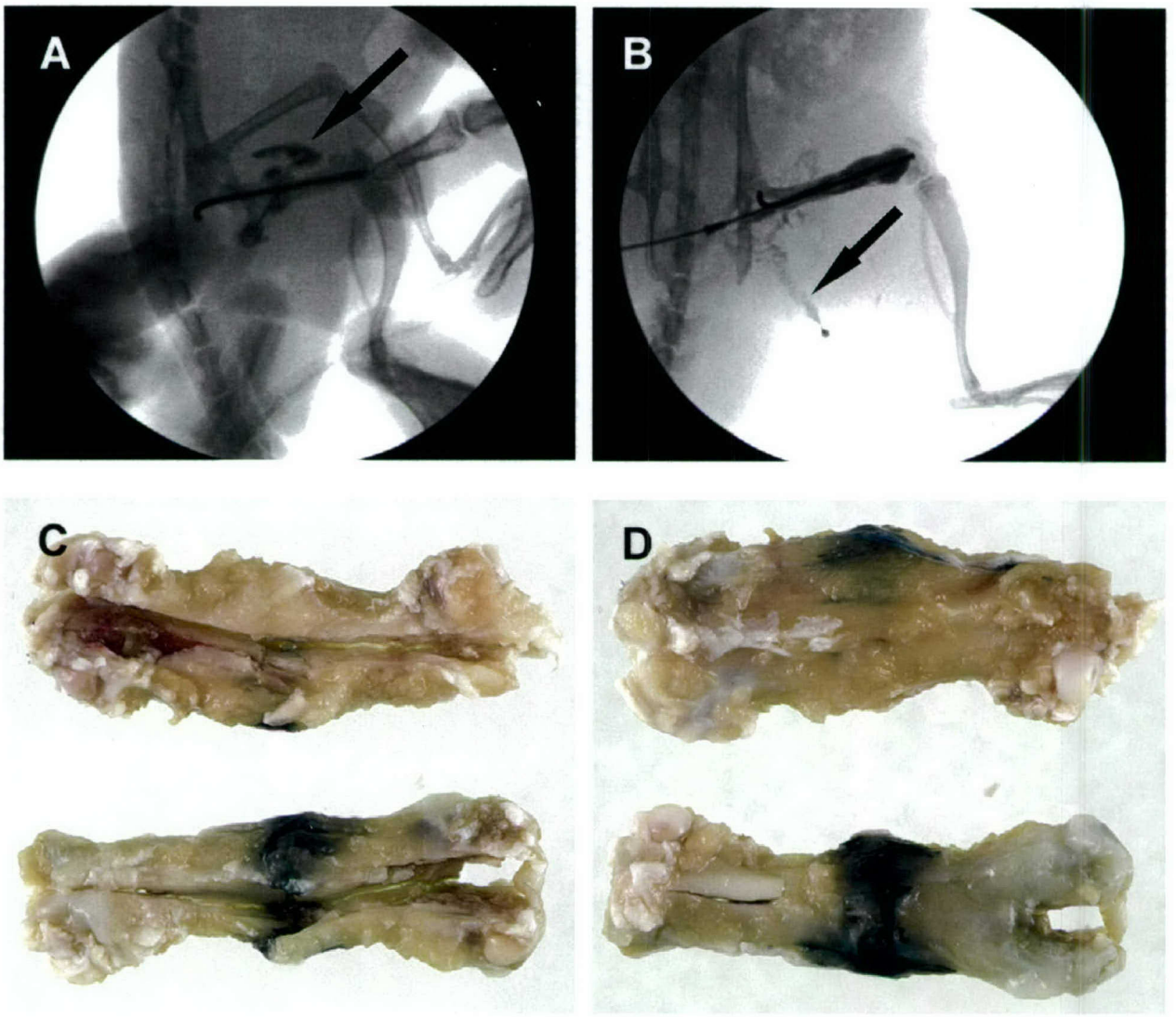



**Figure 5. Marker localization in fractures injected from the exterior (lateral) aspect or through the catheter.**
**TOP: A fluorocscope was used to visualize a radio-opaque contrast dye during a lateral injection (A) or an intramedullary catheter injection (B). Despite best efforts, the dye immediately distributed in the leg muscles when injected from the exterior (A, arrow). When injected through the catheter, the dye was retained in the medullary space (B), except for some leakage visible at the greater trochant a result of normal marrow fluid displacement (arrow).**
**BOTTOM: The MLV-based vector expressing the B-galactosidase marker transgene was injected at one day post-fracture and the femurs harvested at 7 days post-fracture, split open and stained for marker expression. The catheter injection (C, D, bottom) produced more extensive and symmetric marker expression in the interior (C) and exterior (D) of the fracture than the lateral injection (C, D, top).**

that had been injured by the fracture technique and induced to proliferation. Such proliferation rendered them susceptible to MLV-based vector transduction of the BMP-2/4 gene that subsequently differentiated them to cartilage and bone. Although we have determined that this ectopic bone eventually remodels, the therapeutic benefits of tissues outside the periosteum, where fracture healing is normally mediated, are questionable. In contrast, this problem was avoided when the vector was injected through the catheter into the intramedullary space at the fracture site. In this case the bony tissues that developed were not only confined to subperiosteal tissues, but also filled the fracture gap at all times during healing (Figure 6b, d, f, h). The bony tissues appeared after one week of healing, the time when BMP-4 normally differentiates soft callus to bone, suggesting that the temporal BMP-4 gene expression was normal. Higher resolution X-ray and histologic examination of the fracture tissues of individual bones at 14 days (Figure 7a, b) and 28 days (Figure 7c, d) revealed that the fracture tissues consisted of normally appearing chondrocytes and osteoid characteristic of fracture repair. The tissue content of the fracture callus was normal, although this augmented tissue was ectopic in the lateral injections (Figure 7a, c) but subperiosteal and normal in the intramedullary catheter injections (Figure 7b, d). The latter method of therapy delivery, therefore, appears to provide symmetric transgene expression localized to the fracture and represents the greatest potential for measuring therapeutic effects of gene therapy. We will confirm BMP-4 gene expression in these tissues by immunohistochemistry.

Comparative analysis of the fracture tissues produced by exterior and intramedullary injections by peripheral quantitative computed tomography (pQCT) was not possible because of the inaccurate exterior injections resulted in large and variable amounts of ectopic bone spread throughout the muscle (Figure 7). However, a torsional method for the mechanical testing of bone strength in response to our gene therapy has been developed (Figure 8). Preliminary examinations have compared a fracture injected with the B-galactosidase control marker gene at 32 days healing with the unfractured contralateral femur from the same animal and established the conditions for torsional testing of our gene therapy. Our therapy will attempt to accelerate the return of the fractured bone to the load capacity and stiffness of an unfractured bone.

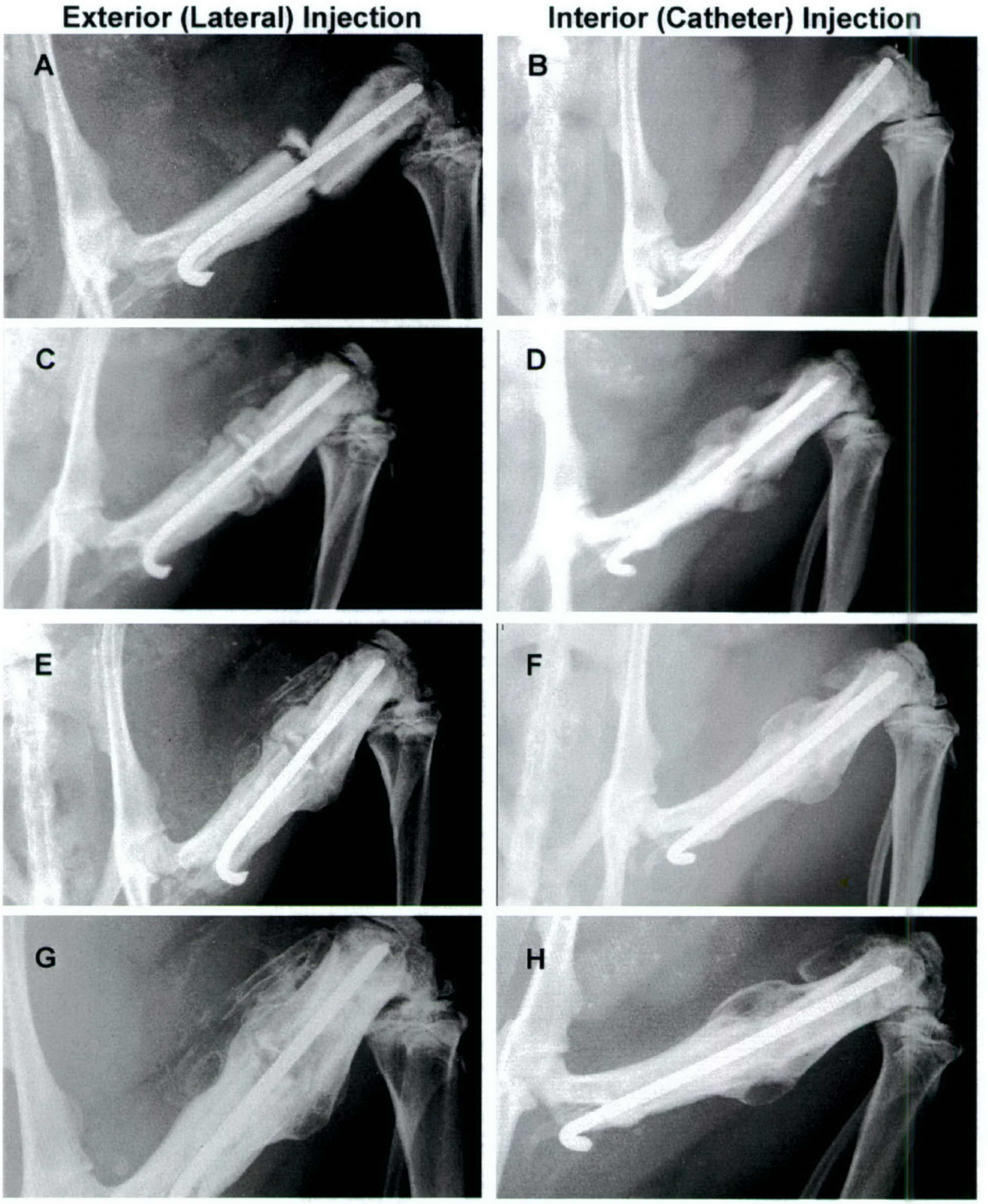



**Figure 6. X-Ray Comparison of Mineralized Tissue During Healing.**
**Injection was performed from the exterior (left) or through the catheter and monitored at 7 days (A,B), 14 days (C,D), 21 days (E,F) and 28 days (G,H) healing. These X-Rays present two different individuals for each injection technique.**

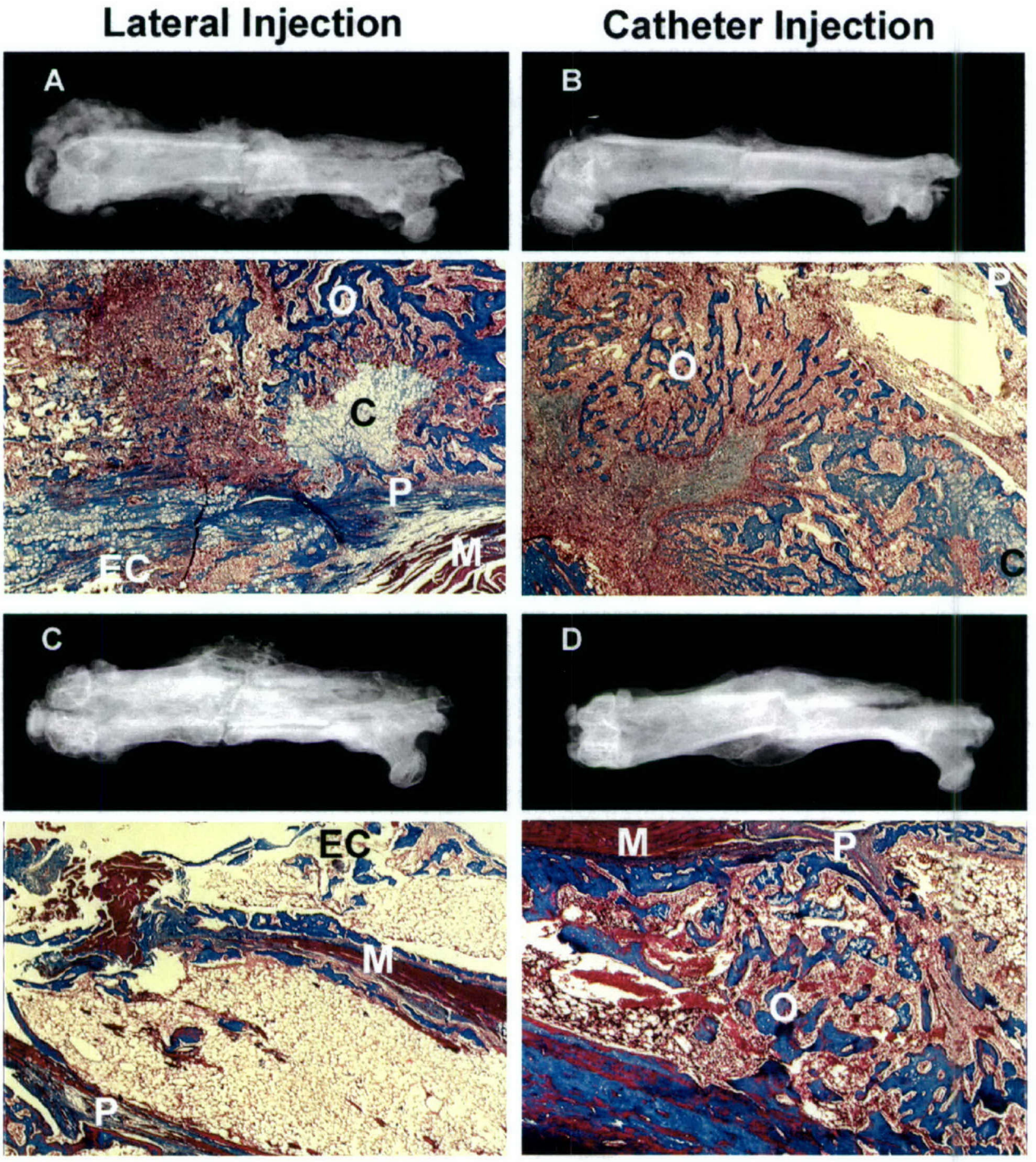



**Figure 7. X-Ray and histology of fracture callus following lateral injection (left) or catheter injection (right) at 14 days (A, B) and 28 days (C, D) healing. Trichrome stains of the fracture callus revealed ectopic (EC) bone formation outside the periosteum (P) at 14 and 28 days in post-fracture lateral injections. Bone formation was under the periosteum (P), at 14 and 28 days in post-fracture catheter injections and did not involve the muscle (M). The fracture tissues appeared normal at all healing times. Cartilage (C), Osteoid (O).**

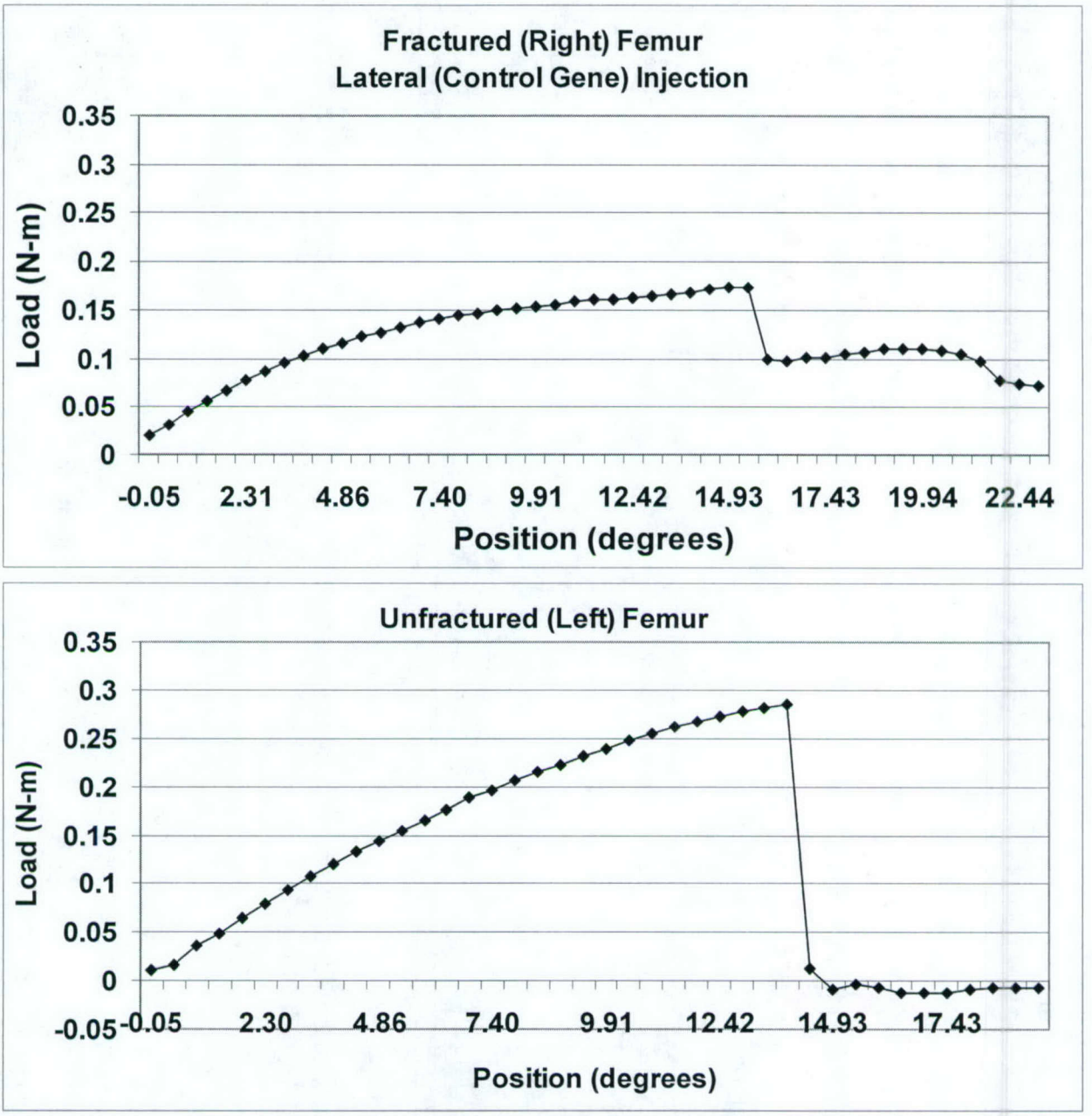



Figure 8. Illustration of the mechanical testing approach for measuring for bone strength. A sample comparison of torsional testing conducted on a rat femur fracture injected with the B-galactosidase (nontherapeutic marker) gene from the lateral aspect and allowed to heal for 32 days (top) as compared with the unfractured contralateral femur from the same animal (bottom). At this time, which is approximately one week prior to bony bridging of the fracture gap, the fracture fails at a slightly larger torsional angle (15 degrees vs. 13 degrees) and approximately 2/3 load (in Newton-meters) of the unfractured femur. These parameters indicate reduced bone stiffness, calculated from the slope of the load vs. angle, and strength, determined by the ultimate load at failure. Such an application of torsional mechanical testing will establish augmentation in response to our gene therapy: the objective is the accelerated return of the fracture torsional strength and stiffness characteristics to that of an unfractured bone.

4) Conclusions

Analysis of injections from the exterior lateral aspect of the fracture demonstrated that extra-periosteal tissues were transduced with the BMP-2/4 transgene, and produced a large and asymmetric mineralized tissue that remained largely outside the periosteal boundaries. In these locations the bony tissues produced by the growth factor could not participate in bony union of the fracture gap, severely limiting the effectiveness of the gene therapy. Intramedullary injection of the MLV vector produced symmetric distribution of transgene expression confined to the periosteal tissues that appeared to augment bony tissues in the fracture gap. As such, this approach maximizes the potential of any therapeutic gene. These results are very conclusive, and we will pursue this technique of vector delivery to determine the efficacy of our different therapeutic genes for fracture healing.

c) Specific Objective 3: To Compare the Superiority of the MLV-based Versus the Lentiviral-based Vector Systems for the BMP-2/4 Transgene

1) Objective

This study will compare the efficacy of the lentiviral and MLV-based vectors for fracture healing. Each will express the BMP-2/4 transgene following delivery using the intramedullary catheter injection. The vector system that exhibits the greatest therapeutic benefits, as determined by bone formation and a return to prefracture mechanical strength, will be used in subsequent combination therapy with multiple transgenes. This study will begin shortly, as the surgical techniques for the vector delivery have just been developed.

d) Specific Objective 4: To Compare the Efficacy of the BMP-2/4 Transgene in the Optimized Vector System with that of the Combination of BMP-2/4 Transgene Plus Another Growth Factor Candidate Gene Identified by Micro-array (see Technical Objective 2)

1) Objective

This study will utilize the gene expression data in the normally healing fracture. *In addition to the microarray analysis of gene expression at 3 days healing originally proposed in Technical Objective 2, Specific Objective 2, we are also analyzing gene expression at 11 days healing.* This approach will provide gene candidates for both early fracture repair and later fracture repair. Work on this study awaits completion of the comprehensive analysis of the microarray gene expression data at these 2 time points. As pathways of gene expression are identified in fracture repair, one or more candidate genes will be selected for combination therapy with the BMP-2/4 transgene.

2. TECHNICAL OBJECTIVE 2: TO APPLY MICROARRAY TO STUDY FRACTURE HEALING

a) Specific Objective 1: To Extend the Number of Genes in Our Current In-house Micro-array Procedure

1) Objective

This study will identify and adapt the experimental microarray chip and analysis system best suited for the analysis of rat fracture gene expression.

2) Materials and Methods

We have adopted the Agilent rat oligomer chip to analyze our fracture RNA in our microarray analysis. This chip has 20,046 gene targets as 60-base oligomers and as such provides a more extensive number of rat gene targets than we are able to achieve with our facilities. Several major families of growth factors, signaling molecules and structural genes are represented, providing one of the most comprehensive surveys of rat gene expression currently available commercially. Most importantly, the "low-input" Agilent dye labeling system allows us to amplify the signal during fluorescent labeling of the cDNA. This approach is highly advantageous for reducing the RNA input into the system, minimizing the numbers of animals used yet maximizing the sensitivity of the microarray analysis for samples with very low amounts of tissues. This is particularly important in the unfractured but pinned control samples of the femur fracture model, which have very little tissue. This labeling system permits us to perform the analysis on these extremely limited samples without pooling the RNA from multiple individuals. We are therefore able to analyze the biological variation between subjects not possible in pooled samples, a problem often ignored in microarray experiments. The Agilent "low input" dye labeling technique was compared with the TSA amplification technique that we have used previously, and with analysis using no amplification. Using 2 ug of RNA for Cy3 and Cy5 dye-labeling, we compared the images following hybridization to the Agilent rat gene chip (below).

3) Results

Below (Figure 9) are scatter plots of the universal RNA labeled with the Agilent amplification protocol and the tyramide signal amplification (TSA) amplification protocol. The data was normalized identically between the arrays as follows, since a Lowess normalization cannot be performed with less than 1000 spots. The plots should give tight clustering around a slope of one since the same universal RNA was labeled using the respective protocols and Cy3 and Cy5 prior to hybridization. For the Agilent low input labeling method, the linear RNA amplification does not introduce artifacts. The only data points lying outside the 2 fold lines are the ratio spike in controls and these follow the expected ratios fairly well (top). The TSA plot (bottom) does not follow the expected slope of one well and the spike in ratio controls are not as consistent as with the Agilent labeling. Each gene's measured intensity was divided by its control channel value in each sample; if the control channel was below 10 then 10 was used instead. If the control channel and the signal channel were both below 10 then no data was reported. All of the genes in each sample were divided by the median of a user-specified list of positive control genes. The median of the positive control genes was calculated using only raw measurements above 10. Of the genes in the positive control list, only genes marked present were used. Positive control genes for normalization included the housekeeping genes glyceraldehydes phosphate dehydrogenase and beta-actin

**Agilent Labeling Low input RNA Amplification Universal RNA for both Cy3 and Cy5 Hybridized to Agilent Rat Gene Chip**

**TSA Labeling Universal RNA for both Cy3 and Cy5 Hybridized to Aigilent Rat Gene Chip**

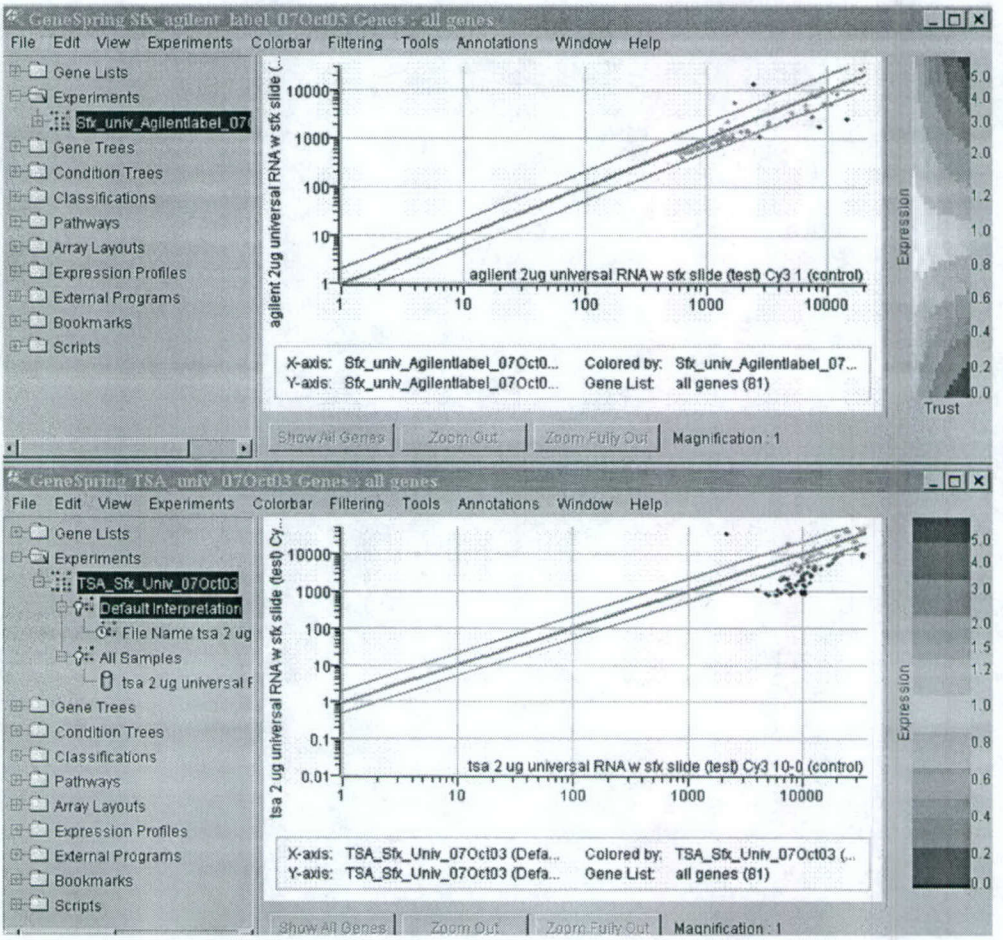



Figure 9. Scatter plot comparison of the Agilent "low input" (top) and TSA (bottom) dye labeling hybridization results on the Agilent rat gene chip.

4) Conclusions

The Agilent "low input" labeling system provides the most sensitive and accurate cDNA labeling system available, and provided superior hybridization images for reproducible analysis of gene expression. We will utilize the Agilent rat gene chip and dye labeling system for our fracture microarray analysis.

b) Specific Objective 2: To Apply Our Extended In-house Microarray to Study Gene Expression in Fracture Callus at 3 Days After Fracture

1) Objective

This study will identify therapeutic gene candidates for fracture gene therapy. Tissues have been harvested for analysis at two time points in healing: 3 days and 11 days. The early time is characteristic of the transition of the inflammatory phase to intramembranous bone formation and was the stated goal for this objective, but we have also included the latter time point, which is characteristic of the maturation of the cartilage intermediate to endochondral bone. Each represents a critical time when fracture repair genes should be expressed and identified in our microarray; the early time point will suggest gene candidates for early clinical

intervention, and the addition of the 11-day data should provide a more comprehensive measurement of gene expression during fracture healing.

2) Materials and Methods

Fracture surgery was performed as described above in Technical Objective 1, Specific Objective 2 (Materials and Methods, Fracture Surgery). The stabilizing pin was inserted and the femur fractured by three-point bending. No catheter was inserted. The control animal femurs were stabilized with an intramedullary pin but not fractured. Because fracture histology in previous studies had identified bone formation around the stabilizing Kirschner wire, this approach controlled for the effects of the stabilization on the healing process.

Femur fracture surgery was performed and RNA isolated from 4 individual fractured femurs at 3 days and 4 individual fractures at 11 days healing, with the fractures compared to equal numbers of individual unfractured (control) femurs at each time point. RNA isolation was performed on pulverized fracture tissues by guanidinium isothiocyanate and phenol extraction (Nemeth et al., 1989). The Cy3 and Cy5 labeling was performed as described in the Agilent "low input" labeling system, and the hybridization performed using equipment and procedures specified in the Agilent 20,046 rat gene chip. We compared each group of fractured RNA and unfractured (but stabilized) control RNA isolates at each time point, 3 days or 11 days post-fracture. Because the Agilent RNA dye labeling system allowed us to analyze fracture and nonfracture gene expression in individual animals, pooling of individual samples was avoided.

Microarray image analysis was also performed in-house, using ScanArray image analysis and Genespring expression analysis software. Lowess normalization was performed to identify differences in the Cy3 or Cy5 dye labeling efficiencies. One-way analysis of variance (ANOVA) established significant changes in expression of up-regulated genes and down-regulated genes for each group of fractured (as compared to unfractured (control)) animals at: 1) 3 days healing; 2) 11 days healing; and 3) additionally, these changes were used to identify combined significant changes in gene expression among all fractured versus nonfractured individuals at 3 days versus 11 days healing.

3) Results

All animals appeared healthy and comfortable, and were mobile at 1 day post-fracture. All fractures were examined at surgery and were midshaft and transverse. All fractures were also examined at sacrifice for evidence of fibrosis due to irritation or migration of the stabilizing pin. None was observed and the fracture callus appeared normal at each harvest time.

The total RNA recovery was routinely 20 ug to 30 ug from fracture tissues and 3 ug to 10 ug from unfractured controls; which had much less tissue than the fractured bone and therefore yielded much less RNA. The bone marrow, another source of nonfracture gene expression, was partially ablated in all animals by removing the pin upon dissection. Spectrophotometric and agarose gel analysis confirmed that the RNA had excellent purity and integrity, respectively.

Venn diagrams (Figures 10, 11 and 12) provide a graphical representation of the statistical analysis of gene expression at 3 days, 11 days, and combined 3 and 11 days healing. Tables 10, 11 and 12, respectively, list the genes that were significantly more than 2-fold up or down-regulated at each of these healing times.

1. At 3 days healing, of the 757 genes with expression differences determined to be significant by ANOVA, 754 genes were more than 2-fold up-regulated, and 3 genes were

**Figure 10: Venn Diagram Illustrating Statistical Analysis of Fracture Gene Expression at 3 Days Healing. Genes with significant changes in expression by ANOVA were compared with genes exhibiting greater than 2-fold changes in expression.**

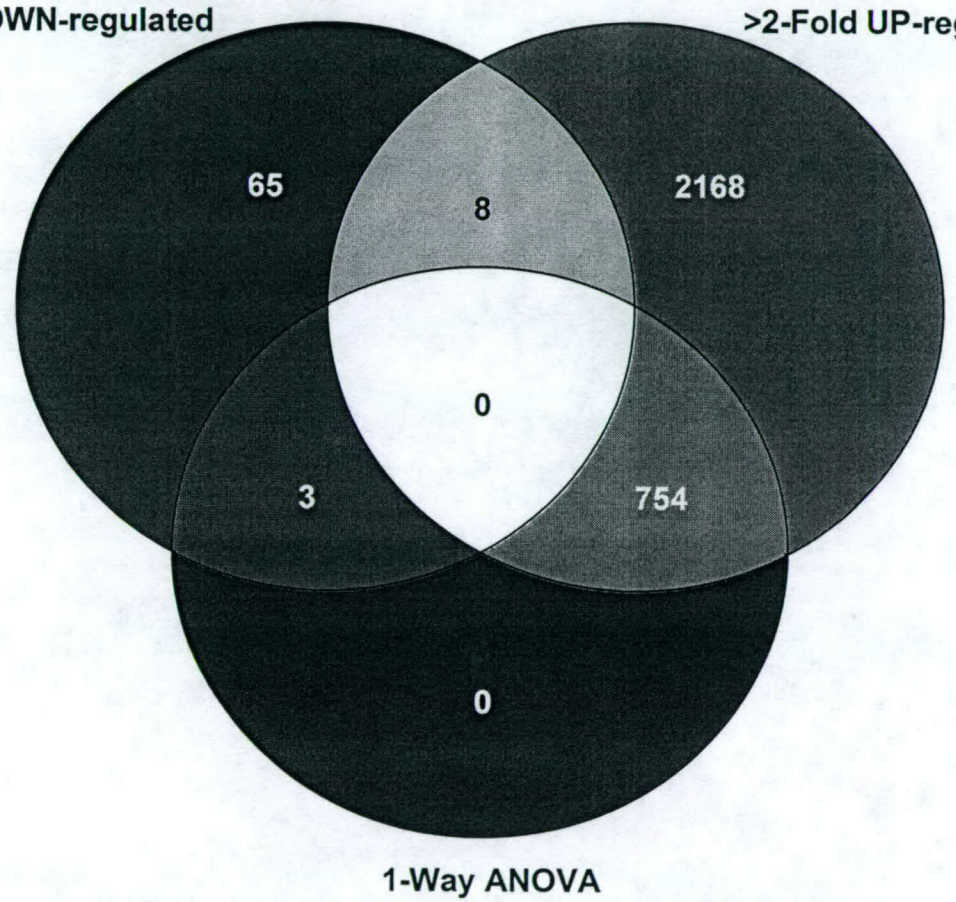


**Figure 11: Venn Diagram Illustrating Statistical Analysis of Fracture Gene Expression at 11 Days Healing. Genes with significant changes in expression by ANOVA were compared with genes exhibiting greater than 2-fold changes in expression.**

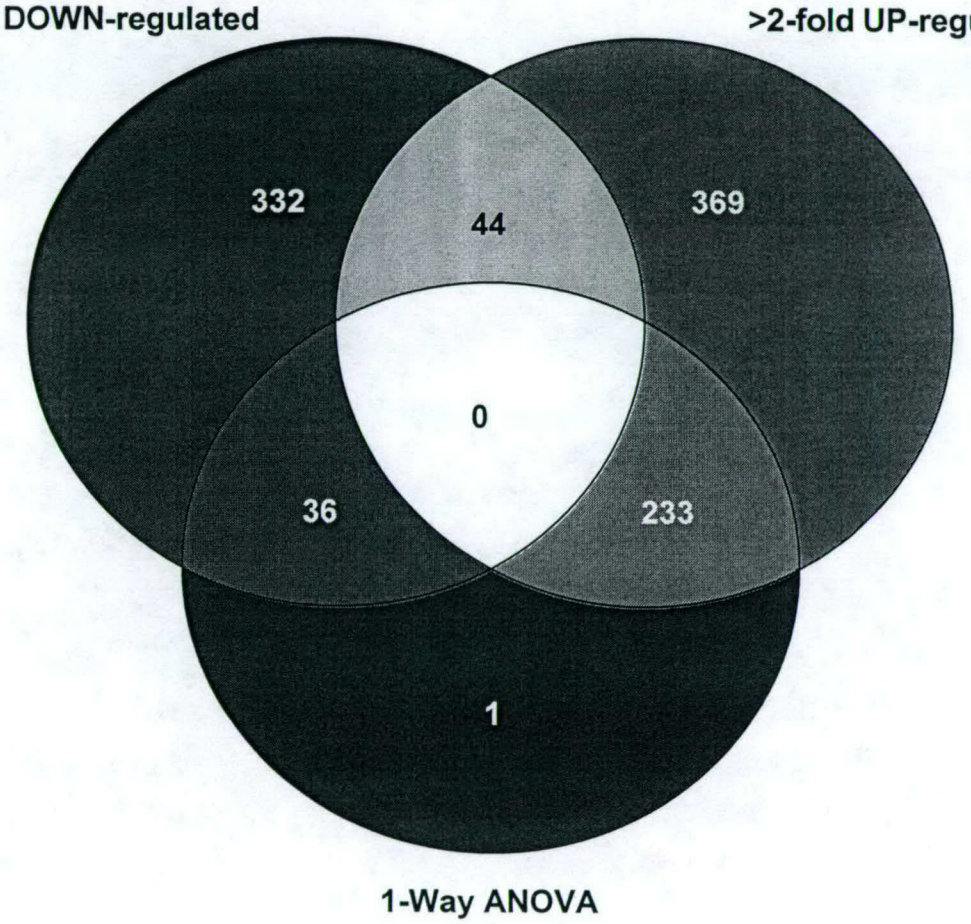
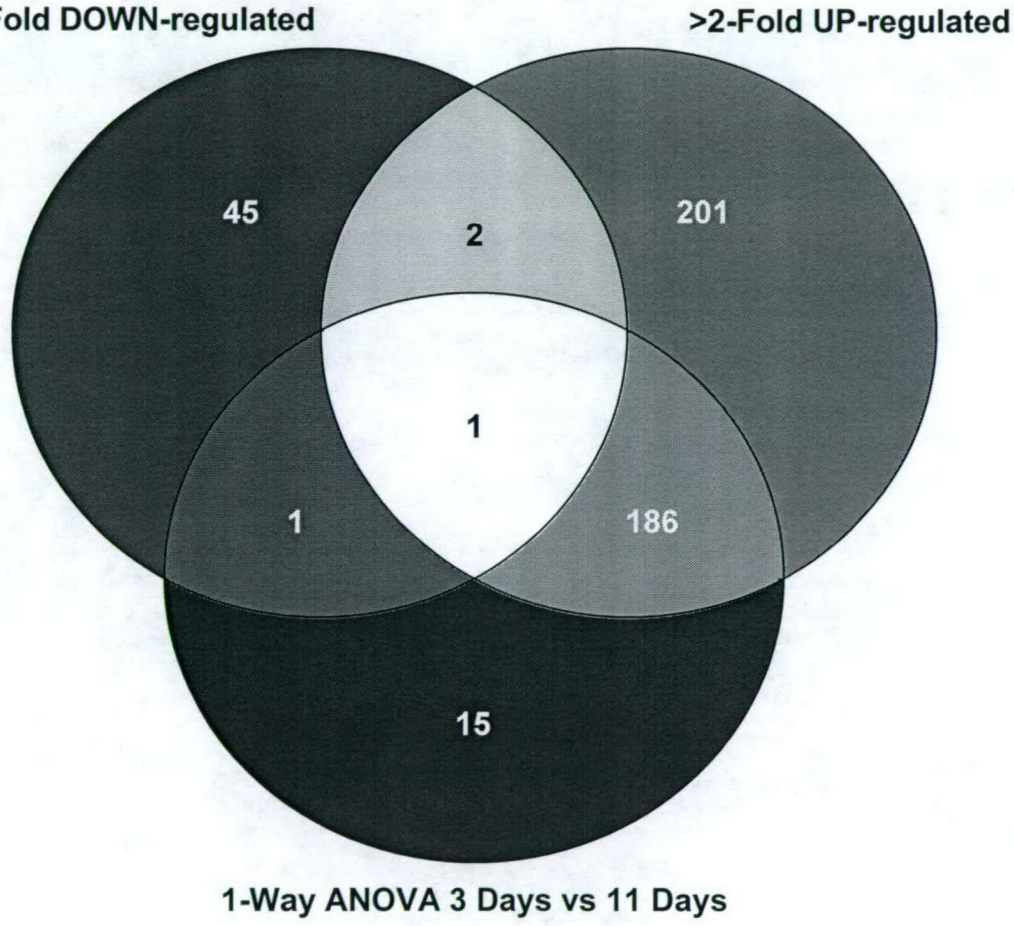


**Figure 12: Venn Diagram Illustrating Statistical Analysis of Fracture Gene Expression at 3 Days and 11 Days Healing. Genes with significant changes in expression by ANOVA were compared with genes exhibiting greater than 2-fold changes in expression.**



more than 2-fold down-regulated. This data is illustrated in the Venn Diagram (Figure 10) and these genes are listed in Table 1 (Appendix).

2. At 11 days healing, of the 270 genes with expression differences determined to be significant by ANOVA, 233 genes were more than 2-fold up-regulated, and 36 genes were more than 2-fold down-regulated. One was less than 2-fold up- or down-regulated. This data is illustrated in the Venn Diagram (Figure 11) and the genes are listed in Table 2 (Appendix).

3. In a comparison of 3 days versus 11 days healing, of the 203 genes with expression differences determined to be significant by ANOVA, 186 were up-regulated 2-fold, 1 was down-regulated 2-fold, and 1 (defensin NP-2, probably involved in inflammation) was biphasic (up-regulated at one time and down-regulated at the other). Additionally, 15 genes were less than 2-fold up- or down-regulated. This data is illustrated in the Venn Diagram (Figure 12) and the genes are listed in Table 3 (Appendix)

The microarray expression data is now being confirmed by real-time RT-PCR using primer pairs selected for 6 of the known genes and 4 of the Expressed Sequence Tags (ESTs). Primers have been ordered and the fracture RNAs used in the microarray are being reverse transcribed for subsequent PCR confirmation.

4) Conclusions

Microarray analysis of fracture healing identified several genes with significant up-regulation or down-regulation in expression at 3 days healing and 11 days healing. These differences in gene expression will provide insights into the gene pathways that participate in fracture healing, and identify therapeutic gene candidates.

c) Specific Objective 3: To Evaluate the Reproducibility and To Analyze the Data from the Extended Micro-array

1) Objectives

During the second 12 months we will focus on reproducibility of the results and data analyses.

1. Additional animals will be included in the microarray analysis to achieve a sample size of at least 5 individuals (fractured and controls) at 3 days and 11 days healing. This approach will extend the analysis microarray reproducibility of identify individual variations in fracture gene expression.

2. We will confirm the gene expression data in the samples analyzed to date by real-time PCR for genes of interest.

3. We will further analyze the microarray gene expression data to functionally classify the genes with changes in expression, identify gene pathways important in fracture healing and include gene candidate(s) in our fracture therapy.

## KEY RESEARCH ACCOMPLISHMENTS

1. We have developed MLV-based and lentiviral-based vector systems for the optimal delivery and expression of therapeutic transgenes to the bone cells of healing fracture tissues.
   a) The MLV-based vector long-terminal repeat (LTR) provides robust nonspecific constitutive expression of the transgene.
   b) Two promoters have been identified for transgene expression from the lentiviral-based vector.
      i) The cytomegalovirus (CMV) promoter provides good nonspecific gene expression.

ii) Surprisingly, the elongation factor-1a (EF-1a) provided optimal gene-specific expression, superior to the collagen promoters and comparable to the CMV promoter.

2. We have optimized surgical procedures to inject the vectors into the interior of the fractured femur through an intramedullary catheter. When compared to simpler injections applied from the exterior aspects of the leg, injection of the BMP-2/4 transgene provided symmetric bone formation within the periosteal layers mediating fracture repair. This system facilitates gene therapy studies by maximizing the effect of the therapy.
3. We have performed microarray analysis on the RNA from four individual fracture subjects at two times of healing to examine global gene expression. Several hundred known and unknown genes are being analyzed to identify potential candidate genes for expression from the optimal vector following application to the fracture by the improved delivery technique.

## REPORTABLE OUTCOMES

There are no reported outcomes as of this date.

## CONCLUSIONS

The development of highly effective gene therapy approaches to musculoskeletal injuries requires the optimization of the components and techniques for the accurate assessment of therapeutic benefits. By identifying which vector and regulatory elements provide the best transgene expression in the bone cells that mediate fracture repair, and by developing vector delivery techniques for optimal therapeutic transgene expression, we have optimized conditions for the accurate evaluation of therapeutic transgene candidates identified by microarray analysis of global gene expression in the normally healing fracture callus. Our previous experience has taught us that if the delivery fails to target expression in suitable cells, even the very robust BMP-2/4 bone forming transgene expressed from an efficient viral vector fails to enhance healing, as measured by bony union of the fracture gap and accelerated return of the bone to prefracture mechanical strength. Other potential therapeutic gene candidates would be expected to fair equally poorly in healing if not targeted accurately. Our studies therefore provide an in vivo system for measuring the therapeutic benefits of a particular fracture gene therapy. We have performed the analysis of global fracture gene expression during early healing (3 days) and later healing (11 days). These data reveal several hundred genes with expression increases or decreases of more than 2-fold at each time after fracture. Current examination of these candidate genes from our microarray will provide an opportunity to utilize these genes and the different aspects of our vectors (i.e., constitutive or gene-specific regulation of expression) for therapies specifically designed for maximum therapeutic benefits in bone repair. Combination gene therapy for individual patients with different musculoskeletal injuries can then be developed.

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## APPENDICES

Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing

Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing

Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and at 11 Days Fracture Healing

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 207864_Rn | 0.049873747 | similar to Mouse lysosome-associated protein, transmembane - 4alpha mRNA, complete cds. |
| BM144069 | 0.04980385 | unknown function |
| BI303540 | 0.049785653 | unknown function |
| NM_012875 | 0.049695275 | Rattus norvegicus Ribosomal protein L39 (Rpl39), mRNA. |
| NM_013181 | 0.049589938 | Rattus norvegicus Protein kinase, cAMP dependent, regulatory, type 1 (Prkar1a), mRNA. |
| 219279_Rn | 0.049411971 | Rattus norvegicus preconditioning-inducible gene 1 protein (PIG-1), mRNA. |
| 218896_Rn | 0.049380843 | Rattus norvegicus general transcription factor IIB (Gtf2b), mRNA. |
| NM_019301 | 0.049372596 | Rattus norvegicus Complement receptor related protein (Cr1), mRNA. |
| BE113476 | 0.049359406 | unknown function |
| 291264_Rn | 0.049330121 | Rattus norvegicus CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 2 (Cd36l2), mRNA. |
| NM_054004 | 0.049328042 | Rattus norvegicus TBP-interacting protein 120A (Tip120A), mRNA. |
| 429753_Rn | 0.049283845 | unknown function |
| NM_053912 | 0.049236423 | Rattus norvegicus pleckstrin homology, Sec7 and coiled/coil domains 3 (Pscd3), mRNA. |
| 221824_Rn | 0.049219301 | similar to Mouse, clone MGC:28735 IMAGE:4460992, mRNA, complete cds. |
| 218445_Rn | 0.049157562 | Rattus norvegicus 3-hydroxy-3-methylglutaryl CoA lyase (Hmgcl), mRNA. |
| 326761_Rn | 0.048991974 | similar to Mouse RING-finger protein MURF mRNA, complete cds. |
| S78556.1 | 0.048987476 | grp75=75 kda glucose regulated protein [rats, Sprague-Dawley, brain, mRNA, 3001 nt]. |
| CB545731 | 0.048634785 | similar to Protein:NP_032846 peptidase 4 [Mus musculus]. score=1.644e-47 |
| NM_139082 | 0.048593301 | Rattus norvegicus BMP and activin membrane-bound inhibitor, homolog (Xenopus laevis) (Bambi), mRNA. |
| 298643_Rn | 0.048580058 | similar to LIM domains containing protein 1 |
| 222433_Rn | 0.048548566 | similar to myosin binding subunit 85 |
| 293026_Rn | 0.048481936 | R.norvegicus c/ebp gamma mRNA. |
| 217465_Rn | 0.048380946 | Rattus norvegicus S-Adenosylmethionine decarboxylase 1A (Amd1a), mRNA. |
| 221020_Rn | 0.048365227 | Rattus norvegicus ribophorin II (Rpn2), mRNA. |
| 221819_Rn | 0.048283134 | similar to mouse CG14164 gene product, clone MGC:36610 IMAGE:5343888, mRNA, complete cds. |
| 223280_Rn | 0.048177796 | Rattus norvegicus Nopp140 associated protein (Nap65), mRNA. |
| NM_022591 | 0.048166166 | Rattus norvegicus telomerase protein component 1 (Tlp1), mRNA. |
| BI292022 | 0.048002822 | unknown function |
| 260322_Rn | 0.047851097 | similar to Protein:NP_473383 tumor endothelial marker 1 precursor [Mus musculus]. score=1.016e-36 |
| 294951_Rn | 0.047799231 | Rat clone RP31-202M22 strain Brown Norway, complete sequence. |
| CB548450 | 0.047677994 | similar to Protein:NP_608219 farnesyl diphosphate synthetase [Mus musculus]. score=1.644e-26 |
| 208505_Rn | 0.047527906 | similar to mouse RIKEN cDNA 5830446M03 gene, clone IMAGE:4039369, mRNA, partial cds. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_012925 | 0.047465077 | Rattus norvegicus CD59 antigen (Cd59), mRNA. |
| BM389346 | 0.047453156 | Rattus norvegicus mRNA for NAD+-specific isocitrate dehydrogenase b-subunit, partial cds. |
| BQ189915 | 0.047447532 | unknown function |
| BM391934 | 0.047122327 | unknown function |
| NM_053826 | 0.047079154 | Rattus norvegicus pyruvate dehydrogenase kinase 1 (Pdk1), mRNA. |
| 205540_Rn | 0.047028693 | Rattus norvegicus latent transforming growth factor beta binding protein 1 (Ltbp1), mRNA. |
| 200837_Rn | 0.047027304 | Rattus norvegicus defensin NP-2 precursor (LOC286995), mRNA. |
| NM_017169 | 0.046996233 | Rattus norvegicus peroxiredoxin 2 (Prdx2), mRNA. |
| 221374_Rn | 0.046804856 | similar to Mouse ras-related protein (rab18) mRNA, complete cds. |
| AI012469 | 0.046513648 | unknown function |
| AA817907 | 0.046294603 | unknown function |
| 223059_Rn | 0.046184462 | Rattus norvegicus thioredoxin (Txn), mRNA. |
| 409590_Rn | 0.04616796 | Rattus norvegicus estrogen-responsive uterine mRNA, partial sequence. |
| CB545716 | 0.046080162 | similar to Translation of nuc:AF394782_1 Homo sapiens rap guanine nucleotide exchange factor mRNA, complete cds; RA-GEF-2. score=7.532e-41 |
| NM_017050 | 0.046057137 | Rattus norvegicus Superoxide dimutase 1, soluble (Sod1), mRNA. |
| 219442_Rn | 0.045950022 | similar to Protein:NP_663355 similar to dendritic cell protein; expressed sequence AL022788; expressed sequence AL024247 [Mus musculus]. score=5.523e-59 |
| 203663_Rn | 0.045824264 | Rat fos-related antigen DNA, exon 4. |
| 218818_Rn | 0.045776893 | similar to mouse f-box and WD-40 domain protein 1B, clone IMAGE:3591748, mRNA, partial cds. |
| 222866_Rn | 0.045761383 | similar to Mouse, SAR1 protein, clone MGC:6113 IMAGE:3585667, mRNA, complete cds. |
| AI101462 | 0.045383821 | unknown function |
| 348275_Rn | 0.045340536 | Rattus norvegicus B-cell translocation gene 1, anti-proliferative (Btg1), mRNA. |
| U21719.1 | 0.045284825 | Rattus norvegicus clone D920 intestinal epithelium proliferating cell-associated mRNA sequence. |
| CB547605 | 0.045254131 | unknown function |
| 327032_Rn | 0.045111989 | similar to Mouse mRNA for beta-tropomyosin. |
| NM_053509 | 0.045072099 | Rattus norvegicus zona pellucida glycoprotein 1 (Zp1), mRNA. |
| AI177116 | 0.044962004 | unknown function |
| NM_080910 | 0.044777469 | Rattus norvegicus phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoribosylaminoimidazole succinocarboxamide synthetase (Paics), mRNA. |
| 297831_Rn | 0.044302609 | similar to Protein:NP_081061 ubiquitin-conjugating enzyme E2C; DNA segment, Chr 2, ERATO Doi 695, expressed [Mus musculus]. score=5.976e-81 |
| NM_080902 | 0.044211492 | Rattus norvegicus hypoxia induced gene 1 (Hig1), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_133297 | 0.044191065 | Rattus norvegicus 15-kDa selenoprotein (Sep15-pending), mRNA. |
| NM_024160 | 0.044112116 | Rattus norvegicus cytochrome b558 alpha-subunit (Cyba), mRNA. |
| 222274_Rn | 0.044026874 | Rattus norvegicus Vav 1 oncogene (Vav1), mRNA. |
| BQ191848 | 0.043679324 | unknown function |
| AF036335.1 | 0.043637001 | Rattus norvegicus NonO/p54nrb homolog mRNA, partial cds. |
| 208278_Rn | 0.043630636 | similar to Mouse, exostoses (multiple) 2, clone MGC:11478 IMAGE:3965079, mRNA, complete cds. |
| NM_031811 | 0.043452894 | Rattus norvegicus transaldolase 1 (Taldo1), mRNA. |
| 201982_Rn | 0.043326107 | similar to Mouse hypoxia induced gene 2 (Hig2) mRNA, complete cds. |
| 291322_Rn | 0.043200528 | similar to Mouse mRNA for p50b (identical to LSP1 and pp52), complete cds. |
| 297948_Rn | 0.042853292 | Rat alpha-platelet-derived growth factor receptor mRNA. |
| 348547_Rn | 0.042706146 | platelet-derived growth factor A-chain (PDGF A-chain) 5 region [rats, marcrophage, mRNA Partial, 486 nt]. |
| NM_023972 | 0.042565763 | Rattus norvegicus glutamate transporter EAAC1 interacting protein (Eaac1), mRNA. |
| NM_133406 | 0.042514003 | Rattus norvegicus 1-acylglycerol-3-phosphate O-acyltransferase 1 (lysophosphatidic acid acyltransferase, delta) (Agpat4), mRNA. |
| NM_031785 | 0.042473435 | Rattus norvegicus ATPase, H+ transporting, lysosomal (vacuolar proton pump), subunit 1 (Atp6s1), mRNA. |
| 296104_Rn | 0.042264073 | similar to Mouse SNAG1 (Snag1) mRNA, complete cds. |
| 220651_Rn | 0.042217538 | Rattus norvegicus Ornitine decarboxylase (Odc1), mRNA. |
| NM_057132 | 0.042073032 | Rattus norvegicus plysia ras-related homolog A2 (Arha2), mRNA. |
| 297277_Rn | 0.04203232 | similar to Translation of nuc:AK019081_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310010B07, full insert sequence; putative. score=6.513e-45 |
| 216979_Rn | 0.041783945 | similar to Protein:NP_080659 RIKEN cDNA 0610011E17 gene [Mus musculus]. score=3.733e-29 |
| 205353_Rn | 0.041699643 | similar to Protein:NP_543027 lymphocyte antigen 6 complex, locus E ligand; DNA segment, Chr 17, Wayne State University 104, expressed [Mus musculus]. score=1.188e-33 |
| 203666_Rn | 0.041659479 | Rattus norvegicus pyruvate dehydrogenase E1 alpha-like (Pdhal), mRNA. |
| 290852_Rn | 0.041585475 | Rattus norvegicus O6-methylguanine-DNA methyltranferase (Mgmt), mRNA. |
| 293702_Rn | 0.04156856 | similar to Mouse DNA sequence from clone RP23-292E3 on chromosome 11, complete sequence. |
| AI574743 | 0.041542199 | similar to Protein:NP_080888 RIKEN cDNA 1810011O01 gene [Mus musculus]. score=7.027e-44 |
| 219360_Rn | 0.041474699 | similar to Mouse mRNA for alpha-2,3-sialyltransferase, complete cds. |
| NM_012923 | 0.041409323 | Rattus norvegicus Cyclin G1 (Ccng1), mRNA. |
| 219078_Rn | 0.041345294 | Rattus norvegicus Vascular cell adhesion molecule 1 (Vcam1), mRNA. |
| 217664_Rn | 0.041328107 | similar to Protein:NP_083902 RIKEN cDNA 2410004H05 [Mus musculus]. score=5.219e-69 |
| AA819021 | 0.041273904 | similar to emb\|X97042\|MMUBCM4GN M.musculus UBcM4 mRNA, mRNA sequence. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 220518_Rn | 0.041231515 | Rattus norvegicus succinate-CoA ligase, GDP-forming, alpha subunit (Suclg1), mRNA. |
| 231197_Rn | 0.041001706 | similar to Mouse DNA sequence from clone RP23-381K21 on chromosome 1, complete sequence. |
| 221045_Rn | 0.040981675 | Rattus norvegicus Proteasome (prosome, macropain) subunit, beta type, 8 (low molecular mass polypeptide 7) (Psmb8), mRNA. |
| 203152_Rn | 0.040893457 | similar to Mouse, clone MGC:8206 IMAGE:3590908, mRNA, complete cds. |
| 221154_Rn | 0.04067949 | similar to Translation of nuc:BC023367_1 Mus musculus, Similar to RIKEN cDNA 2410008H17 gene, clone IMAGE:5027413, mRNA, partial cds. score=7.537e-11 |
| 206383_Rn | 0.040665523 | similar to TFIIB related factor hBRF |
| 385112_Rn | 0.040601103 | Rattus norvegicus ABC50 mRNA, partial cds. |
| BQ781673 | 0.040212794 | unknown function |
| CB548411 | 0.040204551 | unknown function |
| AI598434 | 0.040198287 | unknown function |
| 206959_Rn | 0.04013158 | Rat zinc finger binding protein mRNA, complete cds. |
| BF395191 | 0.040056489 | unknown function |
| 337565_Rn | 0.040053185 | similar to Protein:NP_033921 calmodulin binding protein 1 [Mus musculus]. score=1.029e-79 |
| AW530773 | 0.040051594 | similar to Protein:NP_079758 RIKEN cDNA 2810411G23 gene [Mus musculus]. score=6.854e-59 |
| 293536_Rn | 0.039692464 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 2 (Ptpn2), mRNA. |
| U17565.1 | 0.039688277 | Rattus norvegicus intestinal DNA replication protein mRNA, partial cds. |
| 296230_Rn | 0.039633807 | similar to Mouse Strain C57BL6/J chromosome 8 BAC, RP23-290L7, Complete Sequence, complete sequence. |
| BI274544 | 0.039467225 | unknown function |
| 219476_Rn | 0.039428249 | Rattus norvegicus glucocorticoid-induced leucine zipper (Gilz), mRNA. |
| 291222_Rn | 0.039403744 | similar to data source:SPTR, source key:Q21541, evidence:ISS~putative~related to M142.5 PROTEIN |
| 296009_Rn | 0.039397965 | similar to Mouse mRNA for SYT. |
| 223064_Rn | 0.039333158 | Rattus norvegicus Glutamine synthetase (glutamate-ammonia ligase) (Glul), mRNA. |
| 220754_Rn | 0.039282261 | similar to Mouse H2.0-like homeo box gene (Hlx) gene, complete cds. |
| NM_012582 | 0.039096937 | Rattus norvegicus Haptoglobin (Hp), mRNA. |
| 218826_Rn | 0.039064177 | similar to Mouse, RIKEN cDNA 1110015G04 gene, clone MGC:12050 IMAGE:3707759, mRNA, complete cds. |
| Y07557.1 | 0.03895508 | R.norvegicus mRNA for olfactory receptor. |
| NM_012589 | 0.038950497 | Rattus norvegicus Interleukin 6 (interferon, beta 2) (Il6), mRNA. |
| CA503874 | 0.038731861 | unknown function |
| 221183_Rn | 0.038611909 | Rattus norvegicus valosin-containing protein (Vcp), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| AI233262 | 0.038390083 | similar to Protein:NP_077229 RANBP4; EST AA409693 [Mus musculus]. score=1.041e-114 |
| NM_031514 | 0.038297579 | Rattus norvegicus Janus kinase 2 (a protein tyrosine kinase) (Jak2), mRNA. |
| 203092_Rn | 0.038208121 | similar to Mouse chromosome 11a2 clone rp21-434h10 strain 129S6/SvEvTac, complete sequence. |
| BQ211607 | 0.037985594 | unknown function |
| 221825_Rn | 0.037872296 | Rattus norvegicus PKC-delta binding protein (SRBC), mRNA. |
| 220767_Rn | 0.037715724 | Rattus norvegicus solute carrier family 1, member 3 (Slc1a3), mRNA. |
| BE120761 | 0.037671702 | Rat mRNA for beta-tubulin T beta15. |
| NM_021663 | 0.037625764 | Rattus norvegicus NEFA precursor (Nucb2), mRNA. |
| 217773_Rn | 0.037563554 | similar to Mouse mRNA for hypothetical protein (Tes gene). |
| CB546432 | 0.037485823 | similar to Translation of nuc:AX239864_1 Sequence 4 from Patent WO0164905; unnamed protein product. score=1.392e-33 |
| 298362_Rn | 0.037454787 | Rattus norvegicus cysteine rich protein 61 (Cyr61), mRNA. |
| 220105_Rn | 0.037393903 | similar to Protein:NP_079650 RIKEN cDNA 1110008E19 [Mus musculus]. score=6.257e-42 |
| NM_031576 | 0.037315657 | Rattus norvegicus P450 (cytochrome) oxidoreductase (Por), mRNA. |
| 295226_Rn | 0.037080998 | similar to Mouse, RIKEN cDNA 2810039M17 gene, clone MGC:19258 IMAGE:3982076, mRNA, complete cds. |
| 203115_Rn | 0.036943003 | similar to mouse hypothetical protein FLJ22329, clone IMAGE:4023108, mRNA. |
| CB545171 | 0.036937909 | similar to Protein:NP_009148 programmed cell death 10; apoptosis-related protein 15 [Homo sapiens]. score=2.888e-38 |
| 295015_Rn | 0.036857383 | similar to mouse lymphocyte activation-associated protein, clone MGC:30532 IMAGE:5008328, mRNA, complete cds. |
| 221574_Rn | 0.036577653 | Rattus norvegicus syntenin (Sdcbp), mRNA. |
| 203237_Rn | 0.036429976 | Rattus norvegicus kinase D-interacting substance of 220 kDa (Kidins220), mRNA. |
| 296100_Rn | 0.03641603 | unknown function |
| NM_017055 | 0.036387031 | Rattus norvegicus Transferrin (Tf), mRNA. |
| 435288_Rn | 0.036347345 | similar to Mouse DLC-1 (Arhgap7) gene, exons 12, 13, and 14 and complete cds. |
| 216733_Rn | 0.036287823 | similar to Mouse DNA sequence from clone RP23-476D16 on chromosome X, complete sequence. |
| BU758349 | 0.036258208 | unknown function |
| 218982_Rn | 0.03613097 | Rattus norvegicus Interleukin 6 receptor (Il6r), mRNA. |
| 201441_Rn | 0.035968676 | Rat mRNA for dihydrolipoamide succinyltransferase. |
| 298972_Rn | 0.035914889 | unknown function |
| 297984_Rn | 0.035902433 | similar to mouse hypothetical protein FLJ10647, clone MGC:36197 IMAGE:3964022, mRNA, complete cds. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| AW915841 | 0.035781569 | unknown function |
| 217477_Rn | 0.03574078 | Rattus norvegicus prostaglandin F2 receptor negative regulator (Ptgfrn), mRNA. |
| BQ209715 | 0.035576904 | unknown function |
| 220427_Rn | 0.035481495 | similar to Mouse, clone IMAGE:3991175, mRNA, partial cds. |
| 347777_Rn | 0.035335977 | similar to Mouse, RIKEN cDNA 1500031N16 gene, clone MGC:11632 IMAGE:3582724, mRNA, complete cds. |
| 199999_Rn | 0.035307226 | Rat mRNA for ribosomal protein L39. |
| NM_057191 | 0.035220344 | Rattus norvegicus sarcomeric muscle protein (Sarcosin), mRNA. |
| AA925053 | 0.035157646 | similar to gi\|1478204\|emb\|X97490\|MMPNGPROT M.musculus mRNA for PNG protein, mRNA sequence. |
| 222782_Rn | 0.035128971 | Rattus norvegicus heterogeneous nuclear ribonucleoprotein K (Hnrpk), mRNA. |
| BF283659 | 0.0350206 | unknown function |
| AI234016 | 0.035019155 | similar to GCGPROT:MCM4_MOUSE DNA REPLICATION LICENSING FACTOR MCM4 (CDC21 HOMOLOG) (P1-CDC21). score=4.351e-44 |
| NM_130416 | 0.034965935 | Rattus norvegicus annexin A7 (Anxa7), mRNA. |
| 218116_Rn | 0.034962389 | Rattus norvegicus vacuolar proton-ATPase subunit M9.2 (Atp6k), mRNA. |
| 322787_Rn | 0.034849902 | similar to Mouse Sf3b1 mRNA for pre-mRNA splicing factor SF3b 155 kDa subunit, complete cds. |
| 199973_Rn | 0.034715539 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 6 (Ptph6), mRNA. |
| AI233916 | 0.034621057 | unknown function |
| X94509 | 0.034613492 | unknown function |
| 220547_Rn | 0.034539517 | Rattus norvegicus Fumarate hydratase (Fh), mRNA. |
| 223321_Rn | 0.034513757 | Rattus norvegicus NF-E2-related factor 2 (Nfe2l2), mRNA. |
| 384573_Rn | 0.034377536 | Rattus norvegicus maternal G10 transcript (G10), mRNA. |
| 294517_Rn | 0.034339947 | similar to mouse RIKEN cDNA 3830408P04 gene, clone IMAGE:3601026, mRNA, partial cds. |
| AA819350 | 0.034177255 | similar to Translation of nuc:BC022119_1 Mus musculus, clone MGC:37737 IMAGE:5067385, mRNA, complete cds. score=9.304e-55 |
| 295272_Rn | 0.034132278 | unknown function |
| 293680_Rn | 0.033859253 | Rattus norvegicus guanine nucleotide binding protein, alpha 15 (Gna15), mRNA. |
| 297715_Rn | 0.033820132 | Rat mRNA for p34 protein, complete cds. |
| NM_031660 | 0.033651684 | Rattus norvegicus cyclic AMP phosphoprotein, 19 kDa (Arpp19), mRNA. |
| 205764_Rn | 0.03336253 | similar to Mouse cytosolic beta-N-acetylglucosaminidase (Mgea5) mRNA, complete cds. |
| BE117350 | 0.033319145 | unknown function |
| NM_012848 | 0.033229416 | Rattus norvegicus Ferritin subunit H (Fth1), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 208158_Rn | 0.033195242 | Rattus norvegicus solute carrier family 7 (cationic amino acid transporter, y+system), member 7 (Slc7a7), mRNA. |
| BQ192866 | 0.033142974 | unknown function |
| 234932_Rn | 0.033136104 | similar to Translation of nuc:U22437_1 Mus cookii steroid receptor mRNA, partial cds. score=6.427e-41 |
| 295783_Rn | 0.033043832 | Rat UDP-glucose glycoprotein:glucosyltransferase precursor (Uggt) mRNA, complete cds. |
| 217792_Rn | 0.032783322 | unknown function |
| 220185_Rn | 0.03273315 | similar to Protein:NP_598865 expressed sequence AI256693 [Mus musculus]. score=1.873e-41 |
| NM_031056 | 0.032711326 | Rattus norvegicus matrix metalloproteinase 14, membrane-inserted (Mmp14), mRNA. |
| 222663_Rn | 0.032456113 | similar to Mouse, clone MGC:38921 IMAGE:5362560, mRNA, complete cds. |
| 295983_Rn | 0.032377602 | similar to Mouse QKI protein (qkI) gene, alternative splice product, exon 9 and complete cds. |
| 220595_Rn | 0.032352294 | similar to Protein:NP_064681 tumor-suppressing subchromosomal transferable fragment 4; ESTM671070 (Roswell Park); EST AA241958 [Mus musculus]. score=9.712e-44 |
| 219223_Rn | 0.032306843 | Rattus norvegicus nuclear distribution gene C homolog (Aspergillus) (Nudc), mRNA. |
| AI009167 | 0.032302824 | unknown function |
| 222083_Rn | 0.032198023 | similar to Mouse chromosome 10 clone rp21-668b24 strain 129S6/SvEvTac, complete sequence. |
| L25387.1 | 0.032122111 | Rat phosphofructokinase C (PFK-C) mRNA, complete cds. |
| 200279_Rn | 0.032113202 | Rattus norvegicus acidic ribosomal protein P0 (Arbp), mRNA. |
| 222666_Rn | 0.032093234 | Rattus norvegicus liver cytochrome c oxidase subunit VIII (COX-VIII) mRNA, 3 end of cds. |
| NM_031974 | 0.032055465 | Rattus norvegicus clathrin, light polypeptide (Lca) (Clta), mRNA. |
| 215948_Rn | 0.031874071 | similar to Similar to HTPAP protein |
| 208191_Rn | 0.031819911 | Rattus norvegicus guanine nucleotide binding protein gamma 10 subunit mRNA, partial cds. |
| BI275243 | 0.031674894 | similar to Protein:NP_598819 expressed sequence AA409897 [Mus musculus]. score=1.544e-84 |
| AA818093 | 0.031665918 | unknown function |
| 217333_Rn | 0.031433569 | similar to Mouse, clone MGC:6737 IMAGE:3590767, mRNA, complete cds. |
| 220486_Rn | 0.031406025 | unknown function |
| 222092_Rn | 0.031311556 | Rattus norvegicus ferritin light chain 1 (Ftl1), mRNA. |
| 413727_Rn | 0.0310449 | R.rattus mRNA for ribosomal protein L11. |
| 207650_Rn | 0.030874539 | similar to breast cancer associated protein BRAP1 |
| NM_138892 | 0.030791995 | Rattus norvegicus RS21-C6 protein (RS21-C6), mRNA. |
| 200127_Rn | 0.030781858 | Rattus norvegicus Secreted acidic cystein-rich glycoprotein (osteonectin) (Sparc), mRNA. |
| 199918_Rn | 0.030454969 | Rattus norvegicus ribosomal protein L29 (Rpl29), mRNA. GCGEST:BQ205444 |
| 296074_Rn | 0.030438962 | similar to Translation of nuc:AF414190_1 Mus musculus embryonic seven-span transmembrane protein-like protein (J207) mRNA, complete cds. score=2.121e-39 |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_139105 | 0.030392428 | Rattus norvegicus ribonuclease/angiogenin inhibitor (Rnh1), mRNA. |
| BE120644 | 0.030370366 | unknown function |
| CA334630 | 0.030206327 | similar to Protein:NP_083000 RIKEN cDNA 4632403N06 [Mus musculus]. score=1.182e-104 |
| 199497_Rn | 0.030065838 | Rattus norvegicus stearoyl-Coenzyme A desaturase 2 (Scd2), mRNA. |
| NM_021989 | 0.02998075 | Rattus norvegicus tissue inhibitor of metalloproteinase 2 (Timp2), mRNA. |
| 204455_Rn | 0.029967903 | similar to Protein:NP_079660 RIKEN cDNA 1110003P16 gene [Mus musculus]. score=2.735e-64 |
| 204926_Rn | 0.029867939 | similar to Mouse groucho-related protein (Grg2) mRNA, complete cds. |
| NM_022503 | 0.029781852 | Rattus norvegicus cytochrome c oxidase, subunit 7a 3 (Cox7a3), mRNA. |
| NM_013043 | 0.029739688 | Rattus norvegicus Transforming growth factor beta stimulated clone 22 (Tgfb1i4), mRNA. |
| 206040_Rn | 0.029701379 | similar to Mouse thymidine kinase gene, complete cds. |
| 218405_Rn | 0.029699099 | unknown function |
| BM387285 | 0.029677601 | unknown function |
| 205354_Rn | 0.029630758 | Rattus norvegicus peroxiredoxin 4 (Prdx4), mRNA. |
| 199584_Rn | 0.02963003 | similar to Mouse, tumor protein D52, clone MGC:8210 IMAGE:3590969, mRNA, complete cds. |
| BQ211631 | 0.029577151 | unknown function |
| 217299_Rn | 0.029473166 | Rat mRNA for neuron glucose transporter. |
| CA509361 | 0.029323917 | similar to Protein:NP_000875 IMP (inosine monophosphate) dehydrogenase 2; IMP (inosine 5 -phosphate) dehydrogenase-2 [Homo sapiens]. score=5.184e-83 |
| AA875619 | 0.029322804 | unknown function |
| 298704_Rn | 0.029141386 | similar to TSP2=thrombospondin 2 [Mouse, Genomic, 2030 nt, segment 2 of 2]. |
| 291340_Rn | 0.029118517 | Rat jun dimerization protein 2 (jdp-2) mRNA, complete cds. |
| 203647_Rn | 0.028909883 | similar to Protein:NP_075709 RIKEN cDNA 2010106G01 gene [Mus musculus]. score=1.537e-26 |
| AA899819 | 0.028838137 | similar to gi\|57070\|emb\|X05300\|RNRIBI Rat mRNA for ribophorin I, mRNA sequence. |
| 291940_Rn | 0.028778797 | similar to Mouse DNA sequence from clone RP23-317H19 on chromosome X, complete sequence. |
| 218806_Rn | 0.028733811 | Rattus norvegicus regulator of G-protein signaling protein 2 (Rgs2), mRNA. |
| BQ781402 | 0.028721361 | unknown function |
| NM_031789 | 0.028610444 | Rattus norvegicus NF-E2-related factor 2 (Nfe2l2), mRNA. |
| 297796_Rn | 0.028496929 | similar to Mouse DNA sequence from clone RP23-74L9 on chromosome 11, complete sequence. |
| 292843_Rn | 0.028434412 | similar to Mouse, a disintegrin and metalloprotease domain 8, clone MGC:36123 IMAGE:5324943, mRNA, complete cds. |
| AA925418 | 0.028349207 | unknown function |
| BQ205032 | 0.028304612 | unknown function |
| 219697_Rn | 0.028188134 | similar to Mouse chromosome 5 clone rp23-268d19 strain C57BL/6J, complete sequence. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| BU759576 | 0.028088111 | unknown function |
| BQ210493 | 0.027920074 | similar to Protein:NP_080048 dystrobrevin binding protein 1 [Mus musculus]. score=3.223e-91 |
| 206212_Rn | 0.027665648 | Rattus norvegicus actinin alpha 2 associated LIM protein (Pdlim3), mRNA. |
| CB545220 | 0.027577351 | similar to Protein:NP_082359 RIKEN cDNA 2600017H24 [Mus musculus]. score=1.228e-26 |
| NM_138888 | 0.027524435 | Rattus norvegicus transcription factor INI (Loc192246), mRNA. |
| 217006_Rn | 0.027435695 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 1 (Psma1), mRNA. |
| 295692_Rn | 0.02738032 | similar to Mouse mRNA for src-like adaptor protein. |
| 298215_Rn | 0.027317576 | similar to Mouse tumor endothelial marker 8 precursor (Tem8) mRNA, complete cds. |
| NM_022402 | 0.027048908 | Rattus norvegicus acidic ribosomal protein P0 (Arbp), mRNA. |
| NM_031151 | 0.026994764 | Rattus norvegicus malate dehydrogenase mitochondrial (Mor1), mRNA. |
| CA340775 | 0.026951519 | unknown function |
| 217547_Rn | 0.026906478 | Rattus norvegicus Histone H1-0 (H1f0), mRNA. |
| CA509996 | 0.026906349 | unknown function |
| NM_012895 | 0.026837451 | Rattus norvegicus Adenosin kinase (Adk), mRNA. |
| 204841_Rn | 0.026811784 | similar to Mouse, RIKEN cDNA 2510048O06 gene, clone MGC:35726 IMAGE:5375452, mRNA, complete cds. |
| 206085_Rn | 0.026635624 | similar to Mouse MRPL33 mRNA for mitochondrial ribosomal protein L33 (L33mt), complete cds. |
| 206530_Rn | 0.026587343 | Rattus norvegicus UNC-119 homolog (C. elegans) (Uncl19), mRNA. |
| 348004_Rn | 0.026477174 | similar to Mouse heterogenous nuclear ribonucleoprotein A2/B1 (hnRNP A2/B1) mRNA, complete cds. |
| NM_017325 | 0.026474744 | Rattus norvegicus Runt related transcription factor 1 (Runx1), mRNA. |
| 219250_Rn | 0.026377182 | similar to Translation of nuc:X67029_1 B.taurus mRNA for guanylate kinase. score=1.144e-78 |
| BQ203725 | 0.026305021 | R.norvegicus mRNA for hypoxanthine-guanine phosphoribosyltransferase. |
| 328103_Rn | 0.026183539 | Rattus norvegicus stem cell derived neuronal survival protein precursor (Sdnsf), mRNA. |
| BU760017 | 0.025988392 | similar to GCGPROT:Q9UNV9 PUTATIVE RNA HELICASE. score=2.006e-97 |
| 219111_Rn | 0.025722012 | Rattus norvegicus proteasome (prosome, macropain) subunit, beta type, 2 (Psmb2), mRNA. |
| NM_053365 | 0.025711621 | Rattus norvegicus fatty acid binding protein 4 (Fabp4), mRNA. |
| BQ207009 | 0.025690964 | unknown function |
| 220172_Rn | 0.025631959 | Rattus norvegicus -ral simian leukemia viral oncogene homolog A (ras related) (Rala), mRNA. |
| BQ781097 | 0.025596293 | unknown function |
| AI502470 | 0.025491033 | unknown function |
| CA506853 | 0.025484672 | similar to Translation of nuc:BC004667_1 Mus musculus, clone IMAGE:3498604, mRNA, partial cds. score=1.538e-28 |
| 286501_Rn | 0.025459859 | similar to Mouse DNA sequence from clone RP23-151M22 on chromosome 11, complete sequence. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 218104_Rn | 0.025363599 | Rattus norvegicus copper chaperone for superoxide dismutase (Ccs), mRNA. |
| 216246_Rn | 0.025326332 | Rattus norvegicus thioredoxin-like 2 (Txnl2), mRNA. |
| 384113_Rn | 0.025306869 | Rattus norvegicus complement component factor h (Cfh), mRNA. |
| NM_053556 | 0.025139859 | Rattus norvegicus maternal G10 transcript (G10), mRNA. |
| AI171953 | 0.025085186 | Rattus norvegicus putative ionotropic glutamate receptor GLURR-F11694B (Glurr) mRNA, partial cds. |
| NM_053969 | 0.025062582 | Rattus norvegicus G protein pathway suppressor 1 (Gps1), mRNA. |
| NM_012963 | 0.025031751 | Rattus norvegicus high mobility group box 1 (Hmgb1), mRNA. |
| NM_031557 | 0.024876828 | Rattus norvegicus Prostaglandin I2 (prostacyclin) synthase (Ptgis), mRNA. |
| 275389_Rn | 0.02485342 | similar to mouse electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria II), clone MGC:6481 IMAGE:2646522, mRNA, complete cds. |
| 200736_Rn | 0.024851507 | Rattus norvegicus myosin heavy chain, polypeptide 6, cardiac muscle, alpha (Myh6), mRNA. |
| 288722_Rn | 0.024848495 | similar to Mouse mRNA for mPACPL1, complete cds. |
| NM_024351 | 0.0248231 | Rattus norvegicus Heat shock cognate protein 70 (Hsc70), mRNA. |
| 201624_Rn | 0.024557296 | similar to Translation of nuc:BC025529_1 Mus musculus, Similar to splicing factor, arginine/serine-rich 7 (35kD), clone MGC:38287 IMAGE:5342587, mRNA, complete cds. score=7.527e-07 |
| 203101_Rn | 0.024513916 | similar to Mouse, cytochrome c oxidase subunit VIIb, clone MGC:35766 IMAGE:4987472, mRNA, complete cds. |
| 222207_Rn | 0.024236938 | similar to Translation of nuc:BC008511_1 Mus musculus, Similar to eukaryotic translation initiation factor 3, subunit 4 (delta, 44kD), clone MGC:5726 IMAGE:3592537, mRNA, complete cds. score=2.539e-34 |
| L19927.1 | 0.024071364 | Rattus norvegicus (clone gamma-3) ATP synthase gamma-subunit (ATP5c) mRNA, 3 end cds. |
| AI100773 | 0.024017788 | unknown function |
| NM_053319 | 0.023981514 | Rattus norvegicus dynein, cytoplasmic, light chain 1 (Pin), mRNA. |
| 221408_Rn | 0.023731648 | unknown function |
| NM_019259 | 0.02360757 | Rattus norvegicus complement component 1, q subcomponent binding protein (C1qbp), mRNA. |
| 294991_Rn | 0.023583219 | similar to Mouse, eukaryotic translation initiation factor 3, subunit 6 (48kD), clone MGC:36795 IMAGE:3988386, mRNA, complete cds. |
| 348489_Rn | 0.023450656 | similar to Protein:NP_079802 RIKEN cDNA 2310020H20 [Mus musculus]. score=2.503e-66 |
| 290197_Rn | 0.023321534 | similar to evidence:NAS~hypothetical protein~putative |
| NM_138548 | 0.023291982 | Rattus norvegicus expressed in non-metastatic cells 1 (Nme1), mRNA. |
| NM_017281 | 0.02327355 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 4 (Psma4), mRNA. |
| 290927_Rn | 0.023169282 | unknown function |
| 284666_Rn | 0.02295409 | similar to Mouse mRNA for p40phox, complete cds. |
| 221399_Rn | 0.022943249 | Rat mRNA for proteasome subunit RCX, complete cds. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 203486_Rn | 0.022813287 | similar to mouse dysferlin, clone IMAGE:5324940, mRNA, partial cds. |
| 218928_Rn | 0.022687634 | similar to Mouse enhancer of rudimentary homolog mRNA, complete cds. |
| NM_031756 | 0.022629894 | Rattus norvegicus gamma-glutamyl carboxylase (Ggcx), mRNA. |
| 348360_Rn | 0.022597414 | Rattus norvegicus Nogo-A (Rtn4), mRNA. |
| NM_017264 | 0.022513294 | Rattus norvegicus protease (prosome, macropain) 28 subunit, alpha (Psme1), mRNA. |
| 216942_Rn | 0.022373898 | similar to mouse hypothetical protein FLJ14753, clone MGC:25756 IMAGE:3993056, mRNA, complete cds. |
| CB546087 | 0.022319121 | similar to Translation of nuc:AF048695_1 Mus musculus type I alpha phosphatidylinositol-4-phosphate 5-kinase variant (Pip5ka) mRNA, complete cds. score=2.799e-60 |
| NM_019201 | 0.022260752 | Rattus norvegicus C-terminal binding protein 1 (Ctbp1), mRNA. |
| AA858962 | 0.022174933 | Rat retinol-binding protein (RBP) mRNA, partial cds. |
| 206962_Rn | 0.02194767 | similar to Mouse adenylosuccinate synthetase mRNA, complete cds. |
| 219418_Rn | 0.021945732 | similar to Mouse 7 BAC RP23-266F22 (Roswell Park Cancer Institute Mouse BAC Library) complete sequence. |
| 199762_Rn | 0.021771221 | similar to Mouse, nascent-polypeptide-associated complex alpha polypeptide, clone MGC:35995 IMAGE:3992262, mRNA, complete cds. |
| 221202_Rn | 0.021744546 | Rattus norvegicus solute carrier family 2 (facilitated glucose transporter) member 1 (Slc2a1), mRNA. |
| BM387852 | 0.021625873 | unknown function |
| 222626_Rn | 0.021601117 | similar to Translation of nuc:AK017221_1 Mus musculus 10 days neonate intestine cDNA, RIKEN full-length enriched library, clone:5133400M17, full insert sequence; putative. score=1.652e-69 |
| 203454_Rn | 0.0215208 | similar to Protein:NP_035792 TYRO protein tyrosine kinase binding protein; killer cell activating receptor associated protein [Mus musculus]. score=6.358e-41 |
| 218564_Rn | 0.021507687 | similar to Mouse mRNA for mMCM2, complete cds. |
| 296435_Rn | 0.021450941 | Rattus norvegicus glycogenin (Gyg), mRNA. |
| NM_130413 | 0.021431162 | Rattus norvegicus src family associated phosphoprotein 2 (Scap2), mRNA. |
| 296477_Rn | 0.021315583 | similar to Mouse, RIKEN cDNA 2610034B18 gene, clone MGC:38839 IMAGE:5360750, mRNA, complete cds. |
| 216802_Rn | 0.021231781 | Rattus norvegicus Hermansky-Pudlak syndrome (Hps), mRNA. |
| AA955326 | 0.021231683 | similar to gi\|57719\|emb\|X51537\|RRRPS20 Rat mRNA for ribosomal protein S20, mRNA sequence. |
| AB016165.1 | 0.021155007 | Rattus norvegicus Tsc1 mRNA, 5-noncoding region. |
| BM387331 | 0.021126558 | similar to Protein:NP_080594 RIKEN cDNA 2310003F16 gene [Mus musculus]. score=4.646e-36 |
| 322818_Rn | 0.021072777 | similar to Mouse, clone IMAGE:3489640, mRNA. |
| 298068_Rn | 0.020784248 | Rattus norvegicus CCAAT/enhancerbinding, protein (C/EBP) delta (Cebpd), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 201585_Rn | 0.020607092 | similar to Mouse, clone IMAGE:4921359, mRNA. |
| AW434065 | 0.020514706 | unknown function |
| BE128197 | 0.020276357 | similar to Protein:NP_035946 Ras-GTPase-activating protein (GAP<120>) SH3-domain binding protein 2; ras-GTPase-activating protein (GAP<120>) SH3-domain-binding protein 2 [Mus musculus]. score=6.753e-50 |
| 206462_Rn | 0.02024707 | Rat chromosome 6 clone RP31-263K14 strain Brown Norway, complete sequence. |
| 223254_Rn | 0.020198983 | similar to Mouse mRNA for huntingtin interacting protein-2, complete cds. |
| 218113_Rn | 0.020192936 | similar to Protein:NP_033486 ubiquitin-like 1 [Mus musculus]. score=4.828e-52 |
| 291836_Rn | 0.019720075 | similar to Protein:NP_079979 RIKEN cDNA 3930402F23 gene [Mus musculus]. score=5.076e-35 |
| NM_057119 | 0.019584901 | Rattus norvegicus splicing factor, arginine/serine-rich (transformer 2 Drosophila homolog) 10 (Sfrs10), mRNA. |
| 199737_Rn | 0.019555472 | similar to mouse cyclin B2, clone MGC:11566 IMAGE:3156950, mRNA, complete cds. |
| 223058_Rn | 0.019544902 | similar to Protein:NP_064363 heat shock protein 030 [Mus musculus]. score=1.136e-36 |
| 203128_Rn | 0.019480205 | Rattus norvegicus fertility protein SP22 (SP22), mRNA. |
| NA | 0.01938376 | |
| 429760_Rn | 0.019373379 | antiquitin=26g turgor protein homolog [rats, intestinal mucosa, mRNA Partial, 879 nt]. |
| NM_022634 | 0.019337953 | Rattus norvegicus leucocyte specific transcript 1 (Lst1), mRNA. |
| NM_021765 | 0.019321867 | Rattus norvegicus beta prime COP (Copb), mRNA. |
| 218111_Rn | 0.019307362 | similar to Mouse, clone MGC:8028 IMAGE:3586619, mRNA, complete cds. |
| 218793_Rn | 0.019282319 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 4 (Psma4), mRNA. |
| 297791_Rn | 0.019264057 | similar to cyclin-dependent kinase inhibitor 3 |
| BM383514 | 0.01897211 | unknown function |
| 218610_Rn | 0.018957181 | similar to Mouse, clone IMAGE:5011849, mRNA. |
| 297800_Rn | 0.018890147 | Rattus norvegicus outer mitochondrial membrane receptor rTOM20 (LOC2666601), mRNA. |
| NM_031119 | 0.018816911 | Rattus norvegicus Sjogren syndrome antigen B (Ssb), mRNA. |
| NM_017280 | 0.018797168 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 3 (Psma3), mRNA. |
| CB545156 | 0.018729412 | similar to Translation of nuc:AF426024_1 Mus musculus EIA (Serpinb1) mRNA, complete cds; ov-serpin; MNEI-like protein A. score=1.433e-70 |
| AI410339 | 0.018691665 | unknown function |
| 205991_Rn | 0.018682842 | similar to Mouse, RIKEN cDNA 1500002O20 gene, clone MGC:37579 IMAGE:4988361, mRNA, complete cds. |
| NM_019249 | 0.018550463 | Rattus norvegicus protein tyrosine phosphatase, receptor type, F (Ptprf), mRNA. |
| 363623_Rn | 0.018518189 | Rattus norvegicus ATPase, Na+K+ transporting, beta polypeptide 3 (Atp1b3), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 295314_Rn | 0.018509705 | similar to Translation of nuc:BC004064_1 Mus musculus, clone IMAGE:3590584, mRNA, partial cds. score=5.817e-32 |
| 201293_Rn | 0.018332298 | similar to SPF31 |
| BM388494 | 0.018293157 | unknown function |
| NM_019331 | 0.017971422 | Rattus norvegicus Proprotein convertase subtilisin/kexin type 3 (paired basic amino acid cleaving enzyme, furin, membrane associated receptor protein) (Pcsk3), mRNA. |
| 202269_Rn | 0.01787831 | unknown function |
| NM_031112 | 0.017829384 | Rattus norvegicus ribosomal protein S24 (Rps24), mRNA. |
| 216165_Rn | 0.017782638 | similar to Mouse mRNA for ASM-like phosphodiesterase 3a. |
| NM_017277 | 0.017690498 | Rattus norvegicus adaptor protein complex AP-1, beta 1 subunit (Ap1b1), mRNA. |
| NM_013065 | 0.017533846 | Rattus norvegicus Protein phosphatase 1, catalytic subunit, beta isoform (Ppp1cb), mRNA. |
| 217876_Rn | 0.017533391 | similar to Mouse (SRP9) signal recognition particle subunit mRNA, 689bp. |
| NM_012985 | 0.017511332 | Rattus norvegicus NADH ubiquinone oxidoreductase subunit B13 (Ndufa5), mRNA. |
| BQ194792 | 0.017436153 | similar to Protein:NP_079663 RIKEN cDNA 1110021D01 gene [Mus musculus]. score=8.434e-37 |
| 207121_Rn | 0.017350838 | similar to Protein:NP_081115 RIKEN cDNA 1110055E19 [Mus musculus]. score=2.285e-08 |
| 217022_Rn | 0.017269639 | similar to Mouse mRNA for Rab7 protein. |
| 206358_Rn | 0.017225005 | similar to Sushi domain (SCR repeat) containing protein~data source:Pfam, source key:PF00084, evidence:ISS~putative |
| 384793_Rn | 0.017084658 | fibroblast growth factor receptor 1 beta-isoform [Rattus norvegicus=Norway rat, Sprague-Dawley, kidneys, mRNA, 2520 nt]. |
| 218337_Rn | 0.01705073 | similar to Mouse, clone IMAGE:4221113, mRNA. |
| 217960_Rn | 0.016989747 | Rattus norvegicus Sterol carrier protein 2, liver (Scp2), mRNA. |
| 204888_Rn | 0.016872883 | Rat mRNA for T-plastin. |
| 221804_Rn | 0.016826237 | Rattus norvegicus Superoxide dimutase 1, soluble (Sod1), mRNA. |
| 221829_Rn | 0.016441098 | similar to Mouse IQ motif containing GTPase activating protein 1 (Iqgap1) mRNA, complete cds. |
| 329636_Rn | 0.016415667 | Rattus norvegicus heat shock protein 90 beta mRNA, partial sequence. |
| 288315_Rn | 0.016378518 | similar to Translation of nuc:X95906_1 B.taurus mRNA for CPSF (cleavage and polyadenylation specificity factor) 73 kDa subunit; 73 kDa subunit. score=4.234e-81 |
| 217292_Rn | 0.016247993 | Rattus norvegicus sorting nexin 1 (Snx1), mRNA. |
| 201347_Rn | 0.016241167 | Rattus norvegicus Cystatin beta (Cstb), mRNA. |
| 223283_Rn | 0.016119724 | Rattus norvegicus Carboxypeptidase E (Cpe), mRNA. |
| 298840_Rn | 0.016032621 | Rattus norvegicus connective tissue growth factor (Ctgf), mRNA. |
| CB546220 | 0.01593386 | unknown function |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 207079_Rn | 0.015914064 | similar to Mouse clone mgs1-182e11 strain 129/SvJ, complete sequence. |
| 217237_Rn | 0.015871243 | Rattus norvegicus vitamin A-deficient testicular protein 2-like mRNA, partial sequence. |
| 221731_Rn | 0.015868948 | Rattus norvegicus retinoblastoma binding protein 7 (Rbbp7), mRNA. |
| 204302_Rn | 0.015796911 | similar to Translation of nuc:AK010720_1 Mus musculus ES cells cDNA, RIKEN full-length enriched library, clone:2410073P13, full insert sequence; putative. score=0 |
| 217587_Rn | 0.015729616 | Rattus norvegicus D123 gene product (D123), mRNA. |
| 297939_Rn | 0.015724065 | similar to Mouse DNA sequence from clone RP23-278I3 on chromosome 4, complete sequence. |
| NM_017173 | 0.015424301 | Rattus norvegicus serine (or cysteine) proteinase inhibitor, clade H, member 1 (Serpinh1), mRNA. |
| 313371_Rn | 0.015319657 | unknown function |
| 296312_Rn | 0.015311252 | Rattus norvegicus Apolipoprotein B editing protein (Apobec1), mRNA. |
| BE097398 | 0.015189701 | unknown function |
| CA508165 | 0.01518025 | unknown function |
| 200856_Rn | 0.015137468 | similar to Translation of nuc:AF375046_1 Mus musculus ATP-dependent chromatin remodeling protein SNF2H mRNA, complete cds; similar to human SNF2H. score=0 |
| 216407_Rn | 0.015120898 | Rattus norvegicus calpactin I heavy chain (Anxa2), mRNA. |
| 220314_Rn | 0.015075422 | similar to Protein:NP_081403 RIKEN cDNA 2310016C16 [Mus musculus]. score=3.545e-36 |
| 218557_Rn | 0.015061062 | similar to Mouse (Mus musculus domesticus) mitochondrial carrier homolog 2 mRNA, complete cds; nuclear gene for mitochondrial product. |
| 200179_Rn | 0.015034271 | UI-R-A0-be-c-08-0-UI.s1 UI-R-A0 Rattus norvegicus cDNA clone UI-R-A0-be-c-08-0-UI 3 similar to gb\|L12459\|RATLYSOZYM Rat lysozyme gene exons 1-4, complete cds, mRNA sequence. |
| BE104361 | 0.014990979 | Rat CIIDBP (homologous to human SSRP-1 and mouse T160 genes) mRNA, 3 end. |
| 295616_Rn | 0.014933537 | similar to Mouse BCL3 (Bcl3) mRNA, complete cds. |
| 223327_Rn | 0.014910958 | similar to Unknown (protein for IMAGE:3956746) |
| NM_012839 | 0.014818899 | Rattus norvegicus cytochrome c, somatic (Cycs), mRNA. |
| NM_022516 | 0.014816732 | Rattus norvegicus polypyrimidine tract binding protein (Ptb), mRNA. |
| 202313_Rn | 0.014805995 | Rattus norvegicus Cell division cycle control protein 2 (Cdc2a), mRNA. |
| NM_012756 | 0.014519329 | Rattus norvegicus insulin-like growth factor 2 receptor (Igf2r), mRNA. |
| 219126_Rn | 0.014420798 | Rattus norvegicus ribosomal protein S13 (RPS13) mRNA, 3 end. |
| BE126741 | 0.014379768 | Rattus norvegicus clone p9.2 tenascin mRNA, partial cds. |
| 221559_Rn | 0.01435988 | Rattus norvegicus dolichol-phosphate (beta-D) mannosyltransferase 2 (Dpm2), mRNA. |
| NM_133594 | 0.014093826 | Rattus norvegicus SMT3 suppressor of mif two 3 homolog 2 (yeast) (Smt3h2), mRNA. |
| NM_134346 | 0.014078799 | Rattus norvegicus RAP1B, member of RAS oncogene family (Rap1b), mRNA. |
| 215862_Rn | 0.013951178 | similar to Mouse DNA sequence from clone RP23-480B19 on chromosome 13, complete sequence. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 199952_Rn | 0.01387258 | Rattus norvegicus ribosomal protein S17 (Rps17), mRNA. |
| 222334_Rn | 0.013804176 | Rat Rieske iron-sulfur protein mRNA, complete cds. |
| 221318_Rn | 0.013758427 | unknown function |
| BQ208511 | 0.013709766 | unknown function |
| 220377_Rn | 0.013639749 | similar to Mouse, FK506-binding protein 3 (25kD), clone MGC:6631 IMAGE:3492535, mRNA, complete cds. |
| 288484_Rn | 0.013561995 | similar to Translation of nuc:AB037738_1 Homo sapiens mRNA for KIAA1317 protein, partial cds; Start codon is not identified.. score=8.928e-45 |
| NM_031706 | 0.013537243 | Rattus norvegicus ribosomal protein S8 (Rps8), mRNA. |
| 298340_Rn | 0.013513059 | unknown function |
| BQ782951 | 0.013498257 | similar to Translation of nuc:U58888_1 Mus musculus SH3-containing protein SH3P2 mRNA, partial cds; contains SH3 domain and ankyrin repeats. score=2.1e-104 |
| AI712699 | 0.013440739 | unknown function |
| 208234_Rn | 0.013435548 | Rattus norvegicus coronin, actin binding protein 1A (Coro1a), mRNA. |
| 206189_Rn | 0.013342253 | similar to Translation of nuc:AY013699_1 Mus musculus FKSG24 (Fksg24) mRNA, complete cds. score=1.021e-07 |
| 215769_Rn | 0.013296633 | Rattus norvegicus global ischemia induced protein GIIG15B (GIIg15b), mRNA. |
| 222535_Rn | 0.013239693 | Rattus norvegicus peroxiredoxin 2 (Prdx2), mRNA. |
| 297849_Rn | 0.013170786 | similar to Mouse DNA sequence from clone RP23-353J21 on chromosome 11, complete sequence. |
| 220117_Rn | 0.013140271 | similar to Mouse lymphotoxin-beta receptor gene, putative promoter and exons 1,2,3,4,5 and 6, partial cds. |
| 296375_Rn | 0.013048524 | similar to Mouse NUF2R mRNA, complete cds. |
| BE110980 | 0.012934381 | unknown function |
| 219156_Rn | 0.012773536 | unknown function |
| 202441_Rn | 0.012727495 | similar to retinoic acid receptor responder (tazarotene induced) 1 |
| NM_130405 | 0.012690805 | Rattus norvegicus src associated in mitosis, 68 kDa (Sam68), mRNA. |
| NM_017097 | 0.012577901 | Rattus norvegicus Cathepsin C (dipeptidyl peptidase I) (Ctsc), mRNA. |
| NM_022385 | 0.012563775 | Rattus norvegicus ADP-ribosylation factor-like 1 (Arl1), mRNA. |
| NM_133416 | 0.012504606 | Rattus norvegicus BCL2-related protein A1 (Bcl2a1), mRNA. |
| 200838_Rn | 0.012504231 | Rattus norvegicus Actin, gamma 2, smooth muscle, enteric (Actg2), mRNA. |
| 260281_Rn | 0.012456801 | Rat collagenase (UMRCase) mRNA, 3 end. |
| CA509438 | 0.012450221 | unknown function |
| 297861_Rn | 0.012364873 | similar to Sm D2 |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_022592 | 0.012266134 | Rattus norvegicus transketolase (Tkt), mRNA. |
| 298172_Rn | 0.012216327 | similar to mouse growth factor receptor bound protein 10, clone MGC:28740 IMAGE:4481345, mRNA, complete cds. |
| CB548029 | 0.012177883 | similar to Translation of nuc:U55935_1 Canis familiaris tight junction associated protein ZO-1 MDCK (ZO1-MDCK) mRNA, complete cds; Zonula occludens 1, membrane associated guanylate kinase, MDCK; Tight Junction associated protein (MAGUK). score=1.349e-78 |
| 295478_Rn | 0.012121735 | similar to Mouse, RIKEN cDNA 4833419J07 gene, clone MGC:31193 IMAGE:4194996, mRNA, complete cds. |
| 221375_Rn | 0.01211142 | similar to Mouse, clone MGC:18674 IMAGE:4207201, mRNA, complete cds. |
| 201836_Rn | 0.012056347 | Rat mRNA for ribosomal protein L7a. |
| 199390_Rn | 0.012024097 | Rattus norvegicus high mobility group-17 mRNA, 3 untranslated region, partial sequence. |
| 219944_Rn | 0.012006099 | Rat pre-pro-insulin-like growth factor mRNA, class A, 5 end. |
| 293161_Rn | 0.011999199 | Rattus norvegicus rabphilin 3A-like (without C2 domains) (Rph3al), mRNA. |
| NM_013016 | 0.011918091 | Rattus norvegicus Protein tyrosine phosphatase, non-receptor type substrate 1 (SHP substrate 1) (Ptpns1), mRNA. |
| 218402_Rn | 0.011717513 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 2 (Psma2), mRNA. |
| 216197_Rn | 0.01148805 | Rattus norvegicus protein disulfide isomerase related protein (calcium-binding protein, intestinal-related) (Erp70), mRNA. |
| NM_019383 | 0.01129882 | Rattus norvegicus ATP synthase subunit d (Atp5jd), mRNA. |
| 344123_Rn | 0.01129682 | Rattus norvegicus dynein, cytoplasmic, light chain 1 (Pin), mRNA. |
| 217738_Rn | 0.011253014 | similar to Mouse, clone MGC:37328 IMAGE:4975621, mRNA, complete cds. |
| NM_031022 | 0.011249981 | Rattus norvegicus membrane-spanning proteoglycan NG2 (Cspg4), mRNA. |
| NM_017154 | 0.011235599 | Rattus norvegicus xanthine dehydrogenase (Xdh), mRNA. |
| NM_033235 | 0.011047646 | Rattus norvegicus Malate dehydrogenase-like enzyme (Mdhl), mRNA. |
| 217910_Rn | 0.011012779 | Rattus norvegicus karyopherin (importin) alpha 2 (Kpna2), mRNA. |
| NM_012618 | 0.011011304 | Rattus norvegicus S100 calcium-binding protein A4 (S100a4), mRNA. |
| 205623_Rn | 0.011007021 | similar to Mouse piebald deletion region section 2 of 11 of the complete sequence. |
| NM_017152 | 0.010973397 | Rattus norvegicus ribosomal protein S17 (Rps17), mRNA. |
| NM_017087 | 0.010899363 | Rattus norvegicus biglycan (Bgn), mRNA. |
| 323889_Rn | 0.010882876 | similar to Mouse, SH3-domain binding protein 2, clone MGC:11535 IMAGE:3967543, mRNA, complete cds. |
| AI234256 | 0.010870631 | unknown function |
| 282074_Rn | 0.010699953 | similar to CENP-E |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| BU759721 | 0.010617943 | unknown function |
| 219644_Rn | 0.01041486 | similar to mouse px19-like protein, clone MGC:30986 IMAGE:5251367, mRNA, complete cds. |
| NM_053959 | 0.010398549 | Rattus norvegicus myc box dependent interacting protein 1 (Bin1), mRNA. |
| 219704_Rn | 0.0103239 | similar to Mouse, RIKEN cDNA 1810074P22 gene, clone MGC:6997 IMAGE:3155195, mRNA, complete cds. |
| NM_013011 | 0.010153001 | Rattus norvegicus Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide (Ywhaz), mRNA. |
| AI764088 | 0.010143834 | similar to Translation of nuc:AK021181_1 Mus musculus ES cells cDNA, RIKEN full-length enriched library, clone:C330006B10, full insert sequence; putative. score=1.57e-43 |
| 204964_Rn | 0.010142466 | unknown function |
| 293402_Rn | 0.010109723 | similar to Mouse, midnolin, clone MGC:28080 IMAGE:3710931, mRNA, complete cds. |
| 296464_Rn | 0.010047228 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type substrate 1 (Ptpns1), mRNA. |
| 326551_Rn | 0.009996103 | similar to data source:SPTR, source key:P56556, evidence:ISS~homolog to NADH-UBIQUINONE OXIDOREDUCTASE B14 SUBUNIT (EC 1.6.5.3) (EC 1.6.99.3) (COMPLEX I-B14) (CI-B14)~putative |
| BI277487 | 0.00996125 | similar to Protein:NP_056550 damage specific DNA binding protein 1 (127 kDa) [Mus musculus]. score=9.375e-54 |
| 298335_Rn | 0.009955471 | unknown function |
| CA333998 | 0.00993364 | unknown function |
| 280411_Rn | 0.00992095 | similar to Mouse Ig-like receptor PIRA4 (6M7) mRNA, complete cds. |
| 219577_Rn | 0.009831183 | similar to Mouse, clone IMAGE:3500261, mRNA, partial cds. |
| NM_053867 | 0.009787057 | Rattus norvegicus tumor protein, translationally-controlled 1 (Tpt1), mRNA. |
| NM_013220 | 0.009684891 | Rattus norvegicus ankyrin-like repeat protein (Alrp), mRNA. |
| NM_019195 | 0.009615304 | Rattus norvegicus integrin-associated protein (Cd47), mRNA. |
| BQ782938 | 0.00953195 | Rat mRNA for ribosomal protein S27. |
| 205290_Rn | 0.009391507 | similar to Mouse, RIKEN cDNA 2610041P16 gene, clone MGC:11643 IMAGE:3597862, mRNA, complete cds. |
| NM_030835 | 0.009371072 | Rattus norvegicus ribosome associated membrane protein 4 (RAMP4), mRNA. |
| 205973_Rn | 0.009293626 | Rattus norvegicus cathepsin K (Ctsk), mRNA. |
| NM_012605 | 0.009255043 | Rattus norvegicus Myosin, light polypeptide 2, alkali; ventricular, skeletal, slow (Myl2), mRNA. |
| 293672_Rn | 0.009191981 | Rat clone RP31-202M22 strain Brown Norway, complete sequence. |
| AI233144 | 0.009179013 | unknown function |
| 412096_Rn | 0.009168671 | Rattus norvegicus thymosin beta-4 (Tmsb4x), mRNA. GCGEST:BG664919 |
| BF558629 | 0.009139426 | unknown function |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_022506 | 0.009122465 | Rattus norvegicus ribosomal protein L31 (Rpl31), mRNA. |
| 218595_Rn | 0.008984663 | Rattus norvegicus procollagen C-proteinase enhancer protein (Pcolce), mRNA. |
| NM_013059 | 0.008935173 | Rattus norvegicus alkaline phosphatase, tissue-nonspecific (Alpl), mRNA. |
| NM_012562 | 0.008883405 | Rattus norvegicus Fucosidase, alpha-L-1, tissue (Fuca), mRNA. |
| 219309_Rn | 0.008791973 | Rat heme oxygenase gene, complete cds. |
| 294599_Rn | 0.008769885 | similar to Translation of nuc:X81624_1 M.auratus mRNA for Cl1 protein (Cl1-1). score=1.722e-12 |
| 201267_Rn | 0.008744422 | similar to Mouse mRNA for eIF3 p66, complete cds. |
| NM_017160 | 0.008735854 | Rattus norvegicus ribosomal protein S6 (Rps6), mRNA. |
| 220048_Rn | 0.008725565 | similar to Mouse lysosomal thiol reductase IP30 precursor, mRNA, partial cds. |
| 223052_Rn | 0.00868081 | Rattus norvegicus Triosephosphate isomerase 1 (Tpi1), mRNA. |
| 216538_Rn | 0.008673028 | Rattus norvegicus mRNA for NAD+-specific isocitrate dehydrogenase b-subunit, partial cds. |
| 205140_Rn | 0.008664165 | similar to mouse hypothetical protein MGC3133, clone MGC:11596 IMAGE:3965951, mRNA, complete cds. |
| 343399_Rn | 0.00855704 | similar to Mouse, clone MGC:11811 IMAGE:3595770, mRNA, complete cds. |
| 220056_Rn | 0.008431563 | Rattus norvegicus Subtilisin - like endoprotease (Pace4), mRNA. |
| 295525_Rn | 0.008395076 | Rattus norvegicus ATP-binding cassette, sub-family G (WHITE), member 1 (Abcg1), mRNA. |
| NM_022799 | 0.008294507 | Rattus norvegicus nuclear ubiquitous casein kinase 2 (Nucks), mRNA. |
| 221024_Rn | 0.008263018 | similar to Mouse, telomerase binding protein, p23, clone MGC:5681 IMAGE:3489418, mRNA, complete cds. |
| AI577060 | 0.008235996 | unknown function |
| 294679_Rn | 0.008203782 | unknown function |
| 294570_Rn | 0.008158666 | Rattus norvegicus homocysteine respondent protein HCYP2 (Hcyp2), mRNA. |
| 296547_Rn | 0.00813859 | similar to mouse replication factor C (activator 1) 3 (38kD), clone MGC:25594 IMAGE:4015134, mRNA, complete cds. |
| AA945587 | 0.008038106 | unknown function |
| 218472_Rn | 0.007935005 | Rattus norvegicus mRNA for collagen alpha 1 type XI. |
| CB545815 | 0.007634944 | similar to Translation of nuc:AY049776_1 Homo sapiens unr-interacting protein (UNRIP) mRNA, complete cds. score=3.557e-33 |
| NM_053590 | 0.007611677 | Rattus norvegicus proteasome (prosome, macropain) subunit, beta type 1 (Psmb1), mRNA. |
| 297802_Rn | 0.007611231 | unknown function |
| NM_019222 | 0.007608618 | Rattus norvegicus coronin, actin-binding protein, 1B (Coro1b), mRNA. |
| 298647_Rn | 0.00758564 | Rattus norvegicus collagen triple helix repeat containing 1 (Cthrc1), mRNA. |
| 200080_Rn | 0.007544825 | Rattus norvegicus hsp86 gene for heat shock protein 86. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 217105_Rn | 0.007480593 | Rattus norvegicus ATP synthase, H+ transporting, mitochondrial F0 complex, subunit b, isoform 1 (Atp5f1), mRNA. |
| 223206_Rn | 0.007436423 | similar to Mouse AMD1 gene for S-adenosylmethionine decarboxylase, complete cds. |
| BF415205 | 0.00735195 | Rat mRNA fragment for cardiac actin. |
| NM_017166 | 0.007308496 | Rattus norvegicus stathmin 1 (Stmn1), mRNA. |
| 219673_Rn | 0.007258145 | Rattus norvegicus ribosomal protein S23 (Rps23), mRNA. |
| 220755_Rn | 0.007242171 | similar to Hypothetical protein F54A3.5 |
| 223020_Rn | 0.007214581 | similar to Mouse mRNA for sid23p, complete cds. |
| 343608_Rn | 0.007146423 | Rattus norvegicus ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit (Atp5e), mRNA. |
| NM_022699 | 0.007124181 | Rattus norvegicus ribosomal protein L30 (Rpl30), mRNA. |
| NM_031108 | 0.007040259 | Rattus norvegicus ribosomal protein S9 (Rps9), mRNA. |
| NM_017138 | 0.007022981 | Rattus norvegicus laminin receptor 1 (67kD, ribosomal protein SA) (Lamr1), mRNA. |
| NM_053605 | 0.007013728 | Rattus norvegicus sphingomyelin phosphodiesterase 3, neutral (Smpd3), mRNA. |
| 206087_Rn | 0.007013086 | Rattus norvegicus F-actin binding protein b-Nexilin mRNA, complete cds. |
| AA901338 | 0.006962944 | similar to Translation of nuc:X73836_1 O.cuniculus mRNA for eukaryotic intitation factor 2 beta (eIF-2 beta). score=9.897e-75 |
| 200835_Rn | 0.006895106 | Rattus norvegicus cytochrome c oxidase, subunit Va (Cox5a), mRNA. |
| BF419904 | 0.00687554 | R.norvegicus mRNA for parathyroid hormone regulated sequence (92bp). |
| 296501_Rn | 0.006873167 | similar to Mouse, Rac GTPase-activating protein 1, clone MGC:11396 IMAGE:3602242, mRNA, complete cds. |
| AI409191 | 0.006872879 | unknown function |
| 200849_Rn | 0.006816801 | Rattus norvegicus Creatine kinase, muscle form (Ckm), mRNA. |
| 204800_Rn | 0.00679428 | similar to Mouse forkhead-related transcription factor 1C (Foxp1c) mRNA, complete cds. |
| 223267_Rn | 0.00668658 | Rattus norvegicus ribosomal protein S12 (Rps12), mRNA. |
| 344269_Rn | 0.006652106 | Rattus norvegicus sodium-coupled citrate transporter (NaCT), mRNA. |
| NM_022536 | 0.006647137 | Rattus norvegicus cyclophilin B (Ppib), mRNA. |
| 220815_Rn | 0.006584966 | similar to Translation of nuc:AF403037_1 Mus musculus SPRY domain-containing SOCS box protein SSB-2 mRNA, complete cds. score=4.573e-62 |
| CA509937 | 0.006405841 | Rattus norvegicus guanine nucleotide binding protein gamma 10 subunit mRNA, partial cds. |
| 220915_Rn | 0.006390185 | Rattus norvegicus signal peptidase complex (18kD) (Spc18), mRNA. |
| BQ204885 | 0.006378802 | unknown function |
| BQ207103 | 0.00637126 | unknown function |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| CB547489 | 0.006297374 | similar to Translation of nuc:AB067489_1 Homo sapiens mRNA for KIAA1902 protein, partial cds; Start codon is not identified.. score=3.858e-51 |
| 220886_Rn | 0.006286905 | Rattus norvegicus proteasome (prosome, macropain) subunit, alpha type 5 (Psma5), mRNA. |
| BQ207888 | 0.00627139 | similar to Translation of nuc:AK003540_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110007H07, full insert sequence; putative. score=4.746e-14 |
| 222896_Rn | 0.00622519 | Rattus norvegicus CD164 antigen (Cd164), mRNA. |
| 219437_Rn | 0.006223531 | similar to Mouse cysteine-rich intestinal protein (CRIP) mRNA, complete cds. |
| NM_022521 | 0.006182414 | Rattus norvegicus ornithine aminotransferase (Oat), mRNA. |
| NM_031000 | 0.006168032 | Rattus norvegicus aldo-keto reductase family 1, member A1 (Akr1a1), mRNA. |
| BF558699 | 0.00612421 | unknown function |
| 218711_Rn | 0.006051737 | Rattus norvegicus arginase 1, liver (Arg1), mRNA. |
| 223247_Rn | 0.006034867 | Rat mRNA for ribosomal protein S16. |
| AI599332 | 0.00602388 | unknown function |
| 216375_Rn | 0.005949521 | Rat mRNA for epithelial membrane protein-1. |
| 229336_Rn | 0.005945782 | similar to Mouse collagenous repeat-containing sequence of 26kDa protein (CORS26) mRNA, complete cds. |
| NM_053598 | 0.005943352 | Rattus norvegicus diphosphoinositol polyphosphate phosphohydolase type II (Nudt4), mRNA. |
| NM_017153 | 0.005912168 | Rattus norvegicus ribosomal protein S3a (Rps3a), mRNA. |
| 201835_Rn | 0.005879829 | Rattus norvegicus activating transcription factor ATF-4 (Atf4), mRNA. |
| Y16641.1 | 0.005831339 | Rattus norvegicus mRNA for hnRNP protein, partial. |
| 220184_Rn | 0.00580148 | Rattus norvegicus lectin, galactose binding, soluble 1 (Lgals1), mRNA. |
| NM_053610 | 0.005768097 | Rattus norvegicus peroxiredoxin 6 (Prdx6), mRNA. |
| 293162_Rn | 0.00576711 | similar to hypothetical protein FLJ13236 |
| 217954_Rn | 0.005765612 | similar to Mouse fibroblast growth factor inducible gene 14 (FIN14) mRNA, complete cds. |
| 202298_Rn | 0.005695825 | similar to Translation of nuc:BC031262_1 Homo sapiens, Similar to catenin (cadherin-associated protein), alpha 2, clone MGC:39727 IMAGE:5274351, mRNA, complete cds. score=7.84e-45 |
| 200200_Rn | 0.005682601 | similar to Protein:NP_006734 RNA binding motif protein 3 [Homo sapiens]. score=2.622e-16 |
| 221477_Rn | 0.005665553 | Rattus norvegicus peroxiredoxin 1 (Prdx1), mRNA. |
| 216044_Rn | 0.005637257 | similar to Mouse, signal recognition particle 14 kDa (homologous Alu RNA binding protein), clone MGC:36171 IMAGE:5353575, mRNA, complete cds. |
| 222534_Rn | 0.005630136 | similar to Mouse, clone IMAGE:3583970, mRNA, partial cds. |
| 201560_Rn | 0.005584706 | similar to Translation of nuc:AK002214_1 Mus musculus adult male kidney cDNA, RIKEN full-length enriched library, clone:0610005A19, full insert sequence; putative. score=1.142e-28 |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| BQ209028 | 0.005550304 | unknown function |
| BQ208015 | 0.005545714 | similar to Protein:NP_081121 peptidylprolyl isomerase (cyclophilin)-like 1 [Mus musculus]. score=9.871e-82 |
| 222081_Rn | 0.00546514 | R.rattus mRNA for ribosomal protein L8. |
| 435254_Rn | 0.005459533 | unknown function |
| 203776_Rn | 0.005216471 | Rattus norvegicus glycoprotein (transmembrane) nmb (Gpnmb), mRNA. |
| 215841_Rn | 0.005188832 | similar to Mouse DNA sequence from clone RP23-406B13 on chromosome 4, complete sequence. |
| NM_053602 | 0.005150686 | Rattus norvegicus ATP synthase, H+ transporting, mitochondrial F0 complex, subunit F6 (Atp5j), mRNA. |
| 226208_Rn | 0.005104805 | similar to Mouse Strain C57BL6/J chromosome 5 BAC, RP23-61K9, Complete Sequence, complete sequence. |
| 220656_Rn | 0.005095019 | Rattus norvegicus ribosomal protein L10a (Rpl10a), mRNA. |
| NM_022515 | 0.005048616 | Rattus norvegicus ribosomal protein L24 (Rpl24), mRNA. |
| 202815_Rn | 0.005042476 | similar to Mouse, RIKEN cDNA 1300011C24 gene, clone MGC:7169 IMAGE:3257323, mRNA, complete cds. |
| 200476_Rn | 0.004998189 | Rattus norvegicus Calmodulin 2 (phosphorylase kinase, delta) (Calm2), mRNA. |
| 208250_Rn | 0.004980438 | Rattus norvegicus interferon gamma receptor (Ifngr), mRNA. |
| 206584_Rn | 0.004941247 | Rattus norvegicus smooth muscle cell LIM protein (SmLIM) mRNA, complete cds. |
| NM_019299 | 0.004920952 | Rattus norvegicus clathrin, heavy polypeptide (Hc) (Cltc), mRNA. |
| 347198_Rn | 0.004904098 | similar to Mouse, RIKEN cDNA 2310045A07 gene, clone MGC:41044 IMAGE:1397989, mRNA, complete cds. |
| 221755_Rn | 0.004802136 | unknown function |
| 296765_Rn | 0.004747164 | similar to Mouse Nedd4 WW domain-binding protein 4 mRNA, partial cds. |
| 199779_Rn | 0.004745905 | Rat mRNA for the cysteine proteinase inhibitor cystatin C. |
| 218904_Rn | 0.00470795 | similar to KIAA0782 protein |
| M92059.1 | 0.004707921 | Rattus norvegicus adipsin mRNA sequence. |
| 222657_Rn | 0.00469367 | similar to Mouse, RIKEN cDNA 9130413I22 gene, clone MGC:7196 IMAGE:3482091, mRNA, complete cds. |
| AA925693 | 0.004692767 | similar to gi\|202653\|gb\|J00691\|RATACCYB Rat cytoplasmic beta-actin gene, complete cds, mRNA sequence. |
| 385033_Rn | 0.004658736 | Rattus norvegicus high mobility group box 2 (Hmgb2), mRNA. |
| 221686_Rn | 0.004658001 | Rattus norvegicus calponin 3, acidic (Cnn3), mRNA. |
| 203358_Rn | 0.004573301 | Rat c-fos mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 222773_Rn | 0.004501696 | similar to data source:SPTR, source key:O14521, evidence:ISS~homolog to SUCCINATE DEHYDROGENASE [UBIQUINONE] CYTOCHROME B SMALL SUBUNIT, MITOCHONDRIAL PRECURSOR (CYBS)~putative |
| 221601_Rn | 0.004468579 | Rattus norvegicus Fibronectin 1 (Fn1), mRNA. |
| 218034_Rn | 0.004467934 | Rat collagen XVIII mRNA, partial cds. |
| 220565_Rn | 0.004376637 | similar to Translation of nuc:AK003540_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110007H07, full insert sequence; putative. score=4.746e-14 |
| NM_017148 | 0.004371136 | Rattus norvegicus cysteine rich protein 1 (Csrp1), mRNA. |
| 298460_Rn | 0.004289644 | Rattus norvegicus Early growth response 1 (Egr1), mRNA. |
| 218622_Rn | 0.004279089 | similar to Mouse pigment epithelium-derived factor (PEDF) mRNA, complete cds. |
| 220301_Rn | 0.004196862 | similar to mouse RAB31, member RAS oncogene family, clone MGC:7715 IMAGE:3497938, mRNA, complete cds. |
| CB545139 | 0.004114784 | similar to Translation of nuc:S57132_1 COL16A1=type XVI collagen alpha 1 chain [human, placenta, mRNA Partial, 3720 nt]; This sequence comes from Fig. 2; alpha 1 (XVI). score=2.978e-26 |
| NM_031570 | 0.004114166 | Rattus norvegicus ribosomal protein S7 (Rps7), mRNA. |
| 205016_Rn | 0.004009854 | similar to data source:SPTR, source key:O95168, evidence:ISS~homolog to NADH-UBIQUINONE OXIDOREDUCTASE B15 SUBUNIT (EC 1.6.5.3) (EC 1.6.99.3) (COMPLEX I-B15) (CI-B15)~putative |
| 430014_Rn | 0.003999305 | Rat troponin-c mRNA. |
| CA508092 | 0.003951845 | {clone E592/594, estrogen induced gene} [rats, Sprague-Dawleyhypothalamus, mRNA Partial, 183 nt]. |
| BQ189985 | 0.003705459 | Rattus norvegicus high-affinity immunoglobulin gamma Fc receptor I mRNA, partial cds. |
| 199948_Rn | 0.003612093 | Rattus norvegicus Farnesyl diphosphate synthase (Fdps), mRNA. |
| 221395_Rn | 0.003586152 | similar to Protein:NP_080731 RIKEN cDNA 2510049I19 gene [Mus musculus]. score=5.034e-32 |
| 413406_Rn | 0.003583909 | UI-R-A1-eo-f-12-0-UI.s1 UI-R-A1 Rattus norvegicus cDNA clone UI-R-A1-eo-f-12-0-UI 3 similar to gi\|2918669\|dbj\|C86712\|C86712 Mus musculus fertilized egg cDNA 3-end sequence, clone J0231G01, mRNA sequence. |
| 322873_Rn | 0.003526308 | R.rattus mRNA for dermatan sulfate proteoglycan-II (decorin). |
| AA858954 | 0.003512611 | unknown function |
| 292212_Rn | 0.003464036 | Rattus norvegicus Small inducible gene JE (Scya2), mRNA. |
| U75926.1 | 0.003405713 | Rattus norvegicus cytochrome oxidase subunit VIIa mRNA, 5 untranslated region, partial sequence. |
| BE107038 | 0.003379084 | unknown function |
| 322974_Rn | 0.003298478 | similar to Mouse alcohol dehydrogenase Pan1b mRNA, complete cds. |
| 221393_Rn | 0.003285181 | similar to Protein:NP_033145 Sin3-associated polypeptide 18 [Mus musculus]. score=6.753e-59 |
| NM_022179 | 0.003145482 | Rattus norvegicus Hexokinase 3 (Hk3), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| AW525201 | 0.003106061 | unknown function |
| 201953_Rn | 0.003101484 | similar to Mouse EIA (Serpinb1) mRNA, complete cds. |
| 218829_Rn | 0.00305058 | Rat mRNA for ribosomal protein S25. |
| NM_022514 | 0.003049935 | Rattus norvegicus ribosomal protein L27 (Rpl27), mRNA. |
| 287902_Rn | 0.003011509 | similar to Mouse, asporin, clone MGC:41375 IMAGE:1365428, mRNA, complete cds. |
| NM_022510 | 0.002978847 | Rattus norvegicus ribosomal protein L4 (Rpl4), mRNA. |
| BE105985 | 0.002968754 | unknown function |
| NM_013091 | 0.002964753 | Rattus norvegicus Tumor necrosis factor receptor (Tnfr1), mRNA. |
| 413546_Rn | 0.002951621 | Rattus norvegicus mitochondrial voltage dependent anion channel 3 (Vdac3), mRNA. |
| NM_134353 | 0.002932418 | Rattus norvegicus poly(A) binding protein, cytoplasmic 1 (Pabpc1), mRNA. |
| 222544_Rn | 0.00292739 | Rattus norvegicus Cholesterol esterase (pancreatic) (Lipa), mRNA. |
| AA858647 | 0.002913092 | unknown function |
| CA509950 | 0.002889357 | Rattus sp. 3 UTR. |
| 222629_Rn | 0.002799082 | Rattus norvegicus embigin (Emb), mRNA. |
| 413656_Rn | 0.00276803 | Rattus norvegicus heterogeneous nuclear ribonucleoprotein A1 (Hnrpa1), mRNA. |
| 217559_Rn | 0.002739312 | similar to Mouse mRNA for non-histone chromosomal protein HMG-14. |
| 217519_Rn | 0.002657967 | similar to Mouse, clone MGC:37911 IMAGE:5102315, mRNA, complete cds. |
| 219058_Rn | 0.002641218 | Rattus norvegicus S100 calcium-binding protein A9 (calgranulin B) (S100a9), mRNA. |
| NM_021264 | 0.002570467 | Rattus norvegicus ribosomal protein L35a (Rpl35a), mRNA. |
| AA859114 | 0.002550828 | similar to Protein:NP_080712 RIKEN cDNA 1810054O13 [Mus musculus]. score=6.377e-40 |
| NM_054006 | 0.002530758 | Rattus norvegicus unr protein (unr), mRNA. |
| CB545131 | 0.00250167 | similar to Protein:NP_055392 bromodomain containing protein 1; BR140-like gene [Homo sapiens]. score=7.563e-63 |
| CB544878 | 0.002466638 | unknown function |
| 219818_Rn | 0.002446019 | similar to Mouse spermidine/spermine N1-acetyltransferase (SSAT) mRNA, complete cds. |
| 220191_Rn | 0.002428659 | Rattus norvegicus Annexin V (Anx5), mRNA. |
| 220260_Rn | 0.002427494 | Rattus norvegicus fatty acid binding protein 5, epidermal (Fabp5), mRNA. |
| NM_022597 | 0.002421296 | Rattus norvegicus cathepsin B (Ctsb), mRNA. |
| NM_053467 | 0.002307612 | Rattus norvegicus integral membrane protein Tmp21-I (p23) (Tmp21), mRNA. |
| CB548315 | 0.00230335 | similar to Protein:NP_084515 ATP-binding cassette, subfamily G, member 3 [Mus musculus]. score=6.816e-62 |
| 205807_Rn | 0.002255329 | Rattus norvegicus ribosomal protein L24 (Rpl24), mRNA. GCGEST:BG671633 |
| 200663_Rn | 0.002233586 | Rattus norvegicus vimentin (Vim), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 222095_Rn | 0.002223554 | Rattus norvegicus glutathione peroxidase (GSH-PO) mRNA, complete cds. |
| 231072_Rn | 0.002207388 | similar to Mouse, clone IMAGE:3589736, mRNA, partial cds. |
| 217929_Rn | 0.002188342 | similar to Mouse mRNA for reticulocalbin, complete cds. |
| NM_012881 | 0.002185717 | Rattus norvegicus secreted phosphoprotein 1 (Spp1), mRNA. |
| 295729_Rn | 0.002169041 | Rat thymocyte L-CA (leukocyte common antigen) mRNA, 3 flank. |
| NM_013026 | 0.002149256 | Rattus norvegicus Syndecan (Synd1), mRNA. |
| 223588_Rn | 0.002099154 | Rattus norvegicus macrophage galactose N-acetyl-galactosamine specific lectin (Mgl), mRNA. |
| NM_012904 | 0.002044185 | Rattus norvegicus Annexin 1 (p35) (Lipocortin 1) (Anx1), mRNA. |
| CA505434 | 0.00200634 | unknown function |
| NM_053439 | 0.001973018 | Rattus norvegicus RAN, member RAS oncogene family (Ran), mRNA. |
| 287302_Rn | 0.001964941 | Rat mitochondrial H+-ATP synthase alpha subunit mRNA, complete cds. |
| NM_031629 | 0.001964755 | Rattus norvegicus proteasome (prosome, macropain) subunit, beta type 4 (Psmb4), mRNA. |
| 218823_Rn | 0.001949221 | similar to Mouse, clone MGC:28751 IMAGE:4482756, mRNA, complete cds. |
| AA900381 | 0.001917056 | unknown function |
| 218353_Rn | 0.001897489 | Rattus norvegicus Ornithine decarboxylase antizyme (Oaz), mRNA. |
| 221213_Rn | 0.001892114 | Rattus norvegicus Syndecan 1 (Sdc1), mRNA. |
| NM_022697 | 0.001884179 | Rattus norvegicus ribosomal protein L28 (Rpl28), mRNA. |
| 292230_Rn | 0.001862641 | Rattus norvegicus dual specificity phosphatase 6 (Dusp6), mRNA. |
| 199660_Rn | 0.001853378 | Rattus norvegicus ribosomal protein S3a (Rps3a), mRNA. |
| NM_019289 | 0.001842916 | Rattus norvegicus Actin-related protein complex 1b (Arpc1b), mRNA. |
| 221438_Rn | 0.001776963 | similar to mouse RIKEN cDNA 2400003B06 gene, clone MGC:7860 IMAGE:3501295, mRNA, complete cds. |
| 298020_Rn | 0.001729723 | similar to Mouse homeobox gene Prx2 mRNA. |
| 296381_Rn | 0.001721575 | similar to RAB5 interacting protein 3 |
| 206323_Rn | 0.001701615 | Rattus norvegicus integral membrane protein Tmp21-I (p23) (Tmp21), mRNA. |
| AI411057 | 0.001689435 | unknown function |
| 293007_Rn | 0.001653896 | Rattus norvegicus serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1 (Serpine1), mRNA. |
| 292104_Rn | 0.0016529 | similar to Translation of nuc:BC032959_1 Mus musculus, triggering receptor expressed on myeloid cells 2a, clone MGC:40999 IMAGE:1348066, mRNA, complete cds. score=2.498e-69 |
| 217258_Rn | 0.001645597 | Rattus norvegicus ribosomal protein L27 (Rpl27), mRNA. |
| CB547219 | 0.001637272 | unknown function |
| 221942_Rn | 0.001627929 | Rattus norvegicus Cd63 antigen (Cd63), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_012876 | 0.001623056 | Rattus norvegicus Ribosomal protein S29 (Rps29), mRNA. |
| 222590_Rn | 0.001583154 | Rattus norvegicus ribosomal protein L36 (Rpl36), mRNA. |
| NM_017066 | 0.00155346 | Rattus norvegicus Pleiotrophin (Heparine binding factor, Hbnf, in the mouse) (Ptn), mRNA. |
| NM_053291 | 0.00146793 | Rattus norvegicus Phosphoglycerate kinase 1 (Pgk), mRNA. |
| CA508481 | 0.001413241 | unknown function |
| 199927_Rn | 0.001413027 | Rattus norvegicus H3 histone, family 3B (H3f3b), mRNA. |
| NM_138828 | 0.001389949 | Rattus norvegicus Apolipoprotein E, (Apoe), mRNA. |
| 219224_Rn | 0.001388485 | Rattus norvegicus Diazepam binding inhibitor (GABA receptor modulator, acyl-Coenxyme A binding protein) (Dbi), mRNA. |
| 273885_Rn | 0.001385987 | Rattus norvegicus complement component 5, receptor 1 (C5r1), mRNA. |
| CB606336 | 0.001381343 | unknown function |
| 200661_Rn | 0.001376264 | similar to Mouse, clone MGC:6469 IMAGE:2631779, mRNA, complete cds. |
| NM_057144 | 0.001259786 | Rattus norvegicus cysteine-rich protein 3 (Csrp3), mRNA. |
| NM_031105 | 0.00122689 | Rattus norvegicus large subunit ribosomal protein L36a (Rpl36a), mRNA. |
| NM_080698 | 0.001218503 | Rattus norvegicus fibromodulin (Fmod), mRNA. |
| 221153_Rn | 0.001217213 | Rattus norvegicus mRNA for cathepsin Y, partial cds. |
| 222608_Rn | 0.001205378 | similar to Mouse DNA sequence from clone RP24-144L11 on chromosome 4, complete sequence. |
| NM_012771 | 0.001191971 | Rattus norvegicus Lysozyme (Lyz), mRNA. |
| 294206_Rn | 0.001163216 | similar to Mouse strain C57BL/6J basilin mRNA, complete cds. |
| NM_012512 | 0.001117141 | Rattus norvegicus Beta-2-microglobulin (B2m), mRNA. |
| NM_134334 | 0.001087013 | Rattus norvegicus cathepsin D (Ctsd), mRNA. |
| 222867_Rn | 0.001081208 | Rattus norvegicus Benzodiazepin receptor (peripheral) (Bzrp), mRNA. |
| U57362.1 | 0.001077252 | Rattus norvegicus collagen XII alpha 1 (Col12a1) mRNA, partial cds. |
| NM_031103 | 0.001070446 | Rattus norvegicus ribosomal protein L19 (Rpl19), mRNA. |
| 208320_Rn | 0.001030969 | similar to evidence:NAS~hypothetical protein~putative |
| 217893_Rn | 0.001006907 | Rattus norvegicus heat shock 70kD protein 5 (Hspa5), mRNA. |
| NM_012998 | 0.001002391 | Rattus norvegicus Protein disulfide isomerase (Prolyl 4-hydroxylase, beta polypeptide) (P4hb), mRNA. |
| 343323_Rn | 9.61E-04 | similar to Mouse FKBP65 binding protein mRNA, complete cds. |
| NM_031687 | 9.41E-04 | Rattus norvegicus ubiquitin A-52 residue ribosomal protein fusion product 1 (Uba52), mRNA. |
| BQ200384 | 9.00E-04 | unknown function |
| NM_031114 | 8.58E-04 | Rattus norvegicus S-100 related protein, clone 42C (S100A10), mRNA. |
| 199395_Rn | 8.56E-04 | Rattus norvegicus ribosomal protein S11 (Rps11), mRNA. |
| NM_057114 | 8.39E-04 | Rattus norvegicus peroxiredoxin 1 (Prdx1), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_012587 | 7.89E-04 | Rattus norvegicus integrin binding sialoprotein (Ibsp), mRNA. |
| 219516_Rn | 7.81E-04 | Rattus norvegicus calcium binding protein A6 (calcyclin) (S100a6), mRNA. |
| 217733_Rn | 7.67E-04 | similar to Mouse, RIKEN cDNA 1300019I03 gene, clone MGC:6625 IMAGE:3491528, mRNA, complete cds. |
| NM_053843 | 7.24E-04 | Rattus norvegicus Fc receptor, IgG, low affinity III (Fcgr3), mRNA. |
| 413868_Rn | 7.07E-04 | Rattus norvegicus ribosomal protein S8 (Rps8), mRNA. |
| 347975_Rn | 6.64E-04 | similar to Protein:NP_077751 testis expressed gene 189 [Mus musculus]. score=2.117e-116 |
| 296414_Rn | 6.62E-04 | unknown function |
| NM_012992 | 6.56E-04 | Rattus norvegicus Nucleoplasmin-related protein (Nuclear protein B23 (Npm1), mRNA. |
| CB548041 | 6.35E-04 | similar to Protein:NP_663384 similar to cutlet [Mus musculus]. score=1.492e-20 |
| BQ210920 | 6.26E-04 | unknown function |
| NM_019360 | 6.24E-04 | Rattus norvegicus cytochrome oxidase subunit VIc (Cox6c), mRNA. |
| 221680_Rn | 6.21E-04 | Rattus norvegicus ATP synthase, H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein) (Atp5o), mRNA. |
| NM_031101 | 5.97E-04 | Rattus norvegicus ribosomal protein L13 (Rpl13), mRNA. |
| 200356_Rn | 5.85E-04 | Rattus norvegicus alpha-tubulin (Tuba1), mRNA. |
| 221392_Rn | 5.83E-04 | Rattus norvegicus Matrix Gla protein (Mgp), mRNA. |
| 412899_Rn | 5.81E-04 | similar to Mouse Strain C57BL6/J Chromosome X BAC, RP23-64A09, Complete Sequence, complete sequence. |
| NM_131914 | 5.56E-04 | Rattus norvegicus caveolin 2 (Cav2), mRNA. |
| NM_033539 | 5.52E-04 | Rattus norvegicus eukaryotic translation elongation factor 1 alpha 2 (Eef1a2), mRNA. |
| CA507265 | 4.85E-04 | unknown function |
| 208422_Rn | 4.53E-04 | Rattus norvegicus alanyl (membrane) aminopeptidase (Anpep), mRNA. |
| 348054_Rn | 4.53E-04 | Rattus norvegicus gas-5 growth arrest homolog non-translated mRNA sequence. |
| 216413_Rn | 4.32E-04 | Rattus norvegicus ribosomal protein L6 (Rpl6), mRNA. |
| NM_053982 | 4.09E-04 | Rattus norvegicus ribosomal protein S15a (Rps15a), mRNA. |
| 201846_Rn | 3.73E-04 | Rattus norvegicus ribosomal protein L10 (Rpl10), mRNA. GCGEST:BG671435 |
| NM_022674 | 3.70E-04 | Rattus norvegicus H2A histone family, member Z (H2afz), mRNA. |
| 206738_Rn | 3.49E-04 | Rat metallothionein-2 and metallothionein-1 genes, complete cds. |
| BQ191086 | 3.39E-04 | similar to Protein:NP_079785 RIKEN cDNA 2310008M10 gene [Mus musculus]. score=1.467e-63 |
| AW526982 | 3.37E-04 | unknown function |
| 430016_Rn | 2.60E-04 | Rat mRNA for ribosomal protein S19. |
| NM_022226 | 2.50E-04 | Rattus norvegicus protease, cysteine, 1 (legumain) (Prsc1), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 217441_Rn | 2.31E-04 | similar to Mouse, Deleted in split-hand/split-foot 1 region, clone MGC:31011 IMAGE:5251089, mRNA, complete cds. |
| 199802_Rn | 2.23E-04 | Rattus norvegicus ribosomal protein L21 (Rpl21), mRNA. |
| BQ205045 | 1.72E-04 | unknown function |
| 215832_Rn | 1.16E-04 | similar to Mouse, RIKEN cDNA 3110037K17 gene, clone MGC:41407 IMAGE:1496162, mRNA, complete cds. |
| NM_031099 | 1.07E-04 | Rattus norvegicus ribosomal protein L5 (Rpl5), mRNA. |
| NM_031106 | 8.95E-05 | Rattus norvegicus ribosomal protein L37 (Rpl37), mRNA. |
| NM_013156 | 6.41E-05 | Rattus norvegicus Cathepsin L (Ctsl), mRNA. |
| NM_031111 | 4.79E-05 | Rattus norvegicus ribosomal protein S21 (Rps21), mRNA. |
| 199774_Rn | 4.22E-05 | Rat mRNA for ribosomal protein L9. |
| 218377_Rn | 3.17E-05 | Rattus norvegicus large subunit ribosomal protein L36a (Rpl36a), mRNA. |

**Table 1: Significant 2-Fold Gene Expression Changes at 3 Days Fracture Healing**
**Greater than 2-Fold DOWN-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 200837_Rn | 0.047027304 | Rattus norvegicus defensin NP-2 precursor (LOC286995), mRNA. |
| NM_017055 | 0.036387031 | Rattus norvegicus Transferrin (Tf), mRNA. |
| 208234_Rn | 0.013435548 | Rattus norvegicus coronin, actin binding protein 1A (Coro1a), mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 221163_Rn | 0.04976948 | unknown function |
| 298811_Rn | 0.049730247 | Rattus norvegicus Smhs1 protein (Smhs1), mRNA. |
| NM_031007 | 0.049687102 | Rattus norvegicus adenylyl cyclase 2 (Adcy2), mRNA. |
| 207909_Rn | 0.049383069 | unknown function |
| 278459_Rn | 0.048583013 | similar to Mouse Six1 mRNA. |
| BF416270 | 0.048208788 | unknown function |
| NM_012880 | 0.047743033 | Rattus norvegicus Superoxide dimutase 3 (Sod3), mRNA. |
| 384905_Rn | 0.046817862 | similar to Protein:NP_075875 28kD interferon alpha responsive protein [Mus musculus]. score=3.208e-45 |
| BF416262 | 0.046277827 | unknown function |
| CB545303 | 0.045324534 | unknown function |
| 217519_Rn | 0.045083867 | similar to Mouse, clone MGC:37911 IMAGE:5102315, mRNA, complete cds. |
| BQ209192 | 0.044374361 | similar to Translation of nuc:AF454755_1 Mus musculus vitrin (Vit) mRNA, complete cds; vitreous protein. score=8.359e-53 |
| 222428_Rn | 0.044332706 | similar to Mouse brain cDNA, clone MNCb-3527, similar to AF220152 TACC2 (Human). |
| BF546421 | 0.043819681 | unknown function |
| CB546887 | 0.043699317 | unknown function |
| CB546087 | 0.04331835 | similar to Translation of nuc:AF048695_1 Mus musculus type I alpha phosphatidylinositol-4-phosphate 5-kinase variant (Pip5ka) mRNA, complete cds. score=2.799e-60 |
| NM_031016 | 0.041806517 | Rattus norvegicus muscarinic receptor m2 (Chrm2), mRNA. |
| 216328_Rn | 0.041642695 | similar to Mouse nebulin mRNA, partial cds. |
| 219340_Rn | 0.041517835 | Rattus norvegicus fibroblast growth factor 13 (Fgf13), mRNA. |
| 298020_Rn | 0.041331433 | similar to Mouse homeobox gene Prx2 mRNA. |
| 298291_Rn | 0.041096369 | similar to Mouse chromosome 11a2 clone rp21-493n6 strain 129S6/SvEvTac, complete sequence. |
| CB545321 | 0.040977313 | similar to Protein:NP_032635 matrix metalloproteinase 15; Membrane type 2-MMP [Mus musculus]. score=5.754e-39 |
| 409153_Rn | 0.040895411 | similar to data source:SPTR, source key:P70193, evidence:ISS~putative~similar to MEMBRANE GLYCOPROTEIN |
| CB544481 | 0.039919633 | similar to Protein:NP_032623 matrix gamma-carboxyglutamate (gla) protein [Mus musculus]. score=2.363e-21 |
| NM_013043 | 0.039496822 | Rattus norvegicus Transforming growth factor beta stimulated clone 22 (Tgfb1i4), mRNA. |
| 298157_Rn | 0.039362131 | similar to Mouse DNA sequence from clone RP23-206I14 on chromosome 2, complete sequence. |
| M20035.1 | 0.039342648 | Rat prothymosin-alpha mRNA, complete cds. |
| 414372_Rn | 0.038847833 | Rat clone RP31-249D7 strain Brown Norway, complete sequence. |
| 384548_Rn | 0.038617251 | Rattus norvegicus 25 oligoadenylate synthetase (Oas1), mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 216692_Rn | 0.037885779 | similar to hypothetical protein |
| 232193_Rn | 0.037282673 | similar to hypothetical protein |
| CA338396 | 0.036670827 | similar to Protein:NP_077168 RIKEN cDNA 1110003H02 gene [Mus musculus]. score=2.884e-69 |
| BF543297 | 0.036547921 | unknown function |
| CB606202 | 0.035864013 | similar to Protein:NP_036055 CD97 antigen [Mus musculus]. score=1.682e-21 |
| BF555973 | 0.035776136 | unknown function |
| AW531805 | 0.035544976 | similar to Protein:NP_034631 interferon-induced protein with tetratricopeptide repeats 3 [Mus musculus]. score=5.227e-17 |
| 295703_Rn | 0.035289026 | similar to Mouse, clone MGC:29057 IMAGE:3673874, mRNA, complete cds. |
| 221590_Rn | 0.034326135 | Rat adipocyte hormone-sensitive cAMP phosphodiesterase mRNA, complete cds. |
| AI009167 | 0.034159638 | unknown function |
| AA858962 | 0.034087173 | Rat retinol-binding protein (RBP) mRNA, partial cds. |
| 295756_Rn | 0.032958526 | unknown function |
| AA963765 | 0.032631833 | similar to Protein:NP_032786 osteoglycin [Mus musculus]. score=1.428e-105 |
| 288031_Rn | 0.032406741 | Rat mRNA for alternatively spliced smooth muscle myosin heavy chain (clone RAMHC21). |
| 284357_Rn | 0.032365766 | unknown function |
| U44948.1 | 0.031995375 | Rattus norvegicus smooth muscle cell LIM protein (SmLIM) mRNA, complete cds. |
| 218106_Rn | 0.031554825 | Rattus norvegicus Transforming growth factor beta stimulated clone 22 (Tgfb1i4), mRNA. |
| BI288713 | 0.031178518 | unknown function |
| 252842_Rn | 0.031099168 | Rattus norvegicus a disintegrin and metalloproteinase with thrombospondin motifs 1 (ADAMTS-1) (Adamts1), mRNA. |
| 343632_Rn | 0.029970802 | Rattus norvegicus MEGF6 (Egfl3), mRNA. |
| 220300_Rn | 0.029530905 | similar to Mouse interferon regulatory factor 7 (mirf7) mRNA, complete cds. |
| 216084_Rn | 0.029496484 | Rat cAMP-dependent protein kinase inhibitor (PKI) mRNA, complete cds. |
| AI176675 | 0.029457862 | unknown function |
| CB546846 | 0.029185395 | similar to GCGPROT:O43147 KIAA0397 PROTEIN (FRAGMENT). score=2.625e-56 |
| 201856_Rn | 0.02916694 | Rat myoglobin mRNA, complete cds. |
| 222856_Rn | 0.028582738 | similar to Protein:NP_036039 ubiquitin specific protease 18; ubiquitin specific protease 15 [Mus musculus]. score=5.093e-36 |
| 229344_Rn | 0.028431925 | Rattus norvegicus Myogenic factor 6 (herculin) (Myf6), mRNA. |
| AA946444 | 0.028148529 | unknown function |
| BF281839 | 0.02796791 | unknown function |
| NM_053381 | 0.027864753 | Rattus norvegicus ATPase, (Na+)/K+ transporting, beta 4 polypeptide (Atp1b4), mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 294187_Rn | 0.027678647 | unknown function |
| 220377_Rn | 0.027123665 | similar to Mouse, FK506-binding protein 3 (25kD), clone MGC:6631 IMAGE:3492535, mRNA, complete cds. |
| 218621_Rn | 0.026765322 | Rattus norvegicus Carnitine palmitoyltransferase 1 beta, muscle isoform (Cpt1b), mRNA. |
| 221392_Rn | 0.026728454 | Rattus norvegicus Matrix Gla protein (Mgp), mRNA. |
| CA511442 | 0.02637318 | unknown function |
| BE109129 | 0.025396623 | unknown function |
| 322818_Rn | 0.024717226 | similar to Mouse, clone IMAGE:3489640, mRNA. |
| 298362_Rn | 0.024141303 | Rattus norvegicus cysteine rich protein 61 (Cyr61), mRNA. |
| 219784_Rn | 0.023404328 | similar to Mouse cofilin isoform mRNA, complete cds. |
| BE099435 | 0.023368666 | unknown function |
| 283221_Rn | 0.023366021 | similar to mouse RIKEN cDNA 4933425F03 gene, clone MGC:27633 IMAGE:4506472, mRNA, complete cds. |
| 205548_Rn | 0.023098558 | similar to Mouse, matrilin 2, clone MGC:5875 IMAGE:3492881, mRNA, complete cds. |
| BF566263 | 0.022922933 | similar to Translation of nuc:BC027795_1 Mus musculus, Similar to zinc finger protein 294, clone IMAGE:5251357, mRNA, partial cds. score=1.87e-90 |
| AW525918 | 0.022394022 | similar to Translation of nuc:BC018786_1 Homo sapiens, Similar to thrombospondin 3, clone IMAGE:4875844, mRNA, partial cds. score=2.224e-100 |
| 251419_Rn | 0.022361102 | similar to Protein:NP_071710 secreted modular calcium-binding protein 2 [Mus musculus]. score=1.953e-70 |
| 221116_Rn | 0.022359994 | Rattus norvegicus FXYD domain-containing ion transport regulator 6 (Fxyd6), mRNA. |
| BQ209308 | 0.02221918 | Rattus norvegicus partial mRNA for mono (ADP-ribosyl)transferase (ART3 gene). |
| 221824_Rn | 0.021755549 | similar to Mouse, clone MGC:28735 IMAGE:4460992, mRNA, complete cds. |
| AA925141 | 0.021562998 | similar to gi\|2557199\|gb\|AA633985\|AA633985 ac33f04.s1 Stratagene hNT neuron (#937233) Homo sapiens cDNA clone 858271 3, mRNA sequence. |
| 295799_Rn | 0.020824167 | Rattus norvegicus calcium channel, voltage-dependent, alpha2/delta subunit 1 (Cacna2), mRNA. |
| 205857_Rn | 0.020549915 | Rattus norvegicus delta-like homolog (Drosophila) (Dlk1), mRNA. |
| CA338648 | 0.020296265 | unknown function |
| 294332_Rn | 0.019977612 | similar to Mouse DNA sequence from clone RP23-113P22 on chromosome 4, complete sequence. |
| AA850867 | 0.019974476 | similar to Protein:NP_036022 sarcoglycan, gamma (35kD dystrophin-associated glycoprotein) [Mus musculus]. score=3.114e-43 |
| NM_130743 | 0.019919763 | Rattus norvegicus interferon, alpha-inducible protein 27-like (Ifi27l), mRNA. |
| 221410_Rn | 0.019856963 | similar to Mouse gene for neural cell adhesion molecule 3 region exon b; NCAM-120 C-term. |
| AI112095 | 0.019425331 | unknown function |
| 220900_Rn | 0.019352262 | unknown function |
| 200130_Rn | 0.019296916 | Rattus norvegicus troponin T2, cardiac (Tnnt2), mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 384058_Rn | 0.01894611 | similar to Protein:NP_113578 upregulated during skeletal muscle growth 4; DNA segment, Chr 3, Brigham & Womens Genetics 1078 expressed [Mus musculus]. score=4.545e-12 |
| BF401264 | 0.018038843 | unknown function |
| NM_053395 | 0.017720716 | Rattus norvegicus small muscle protein, X-linked (Smpx), mRNA. |
| 298899_Rn | 0.01726424 | unknown function |
| 199765_Rn | 0.017038842 | Rattus norvegicus troponin I, skeletal, fast 2 (Tnni2), mRNA. |
| 206584_Rn | 0.016975793 | Rattus norvegicus smooth muscle cell LIM protein (SmLIM) mRNA, complete cds. |
| NM_016990 | 0.016731409 | Rattus norvegicus Adducin 1, alpha (Add1), mRNA. |
| BQ211970 | 0.015887359 | similar to Protein:NP_057921 tropomodulin 4 [Mus musculus]. score=2.081e-49 |
| 199469_Rn | 0.015109729 | Rattus norvegicus BCL2/adenovirus E1B 19 kDa-interacting protein 3, nuclear gene for mitochondrial product (Bnip3), mRNA. |
| 218120_Rn | 0.015103888 | similar to amylo-1, 6-glucosidase/4-alpha-glucancotransferase |
| 206075_Rn | 0.015062511 | similar to mouse annexin A8, clone MGC:13875 IMAGE:4013266, mRNA, complete cds. |
| 200473_Rn | 0.014578753 | Rattus norvegicus N-myc downstream-regulated gene 2 (Ndrg2), mRNA. |
| 297341_Rn | 0.014561725 | similar to Translation of nuc:S71251_1 monocyte chemotactic protein-3 [mice, macrophage cell line WEHI-3, mRNA, 808 nt]; This sequence comes from Fig. 1; MCP-3; Marc/Fic protein. score=7.81e-42 |
| 221113_Rn | 0.01456035 | Rattus norvegicus small inducible cytokine B subfamily (Cys-X-Cys), member 10 (Scyb10), mRNA. |
| NM_019145 | 0.014553218 | Rattus norvegicus cholinergic receptor, nicotinic, gamma polypeptide (Chrng), mRNA. |
| BI276352 | 0.014349707 | similar to Protein:NP_112019 protein kinase C and casein kinase substrate in neurons 3 [Mus musculus]. score=3.547e-55 |
| 298983_Rn | 0.014075765 | similar to myopalladin |
| 294630_Rn | 0.013775547 | similar to Mouse DNA sequence from clone RP23-391E6 on chromosome 4, complete sequence. |
| 219145_Rn | 0.012507577 | similar to Mouse DNA sequence from clone RP23-141C15 on chromosome 4, complete sequence. |
| AI172305 | 0.012486349 | similar to Translation of nuc:AK009124_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310003M01, full insert sequence; putative. score=8.841e-72 |
| NM_022190 | 0.012316201 | Rattus norvegicus aggrecan 1 (Agc1), mRNA. |
| 200201_Rn | 0.012185791 | Rattus norvegicus ATPase, Ca++ transporting, cardiac muscle, slow twitch 2 (Atp2a2), mRNA. |
| 206087_Rn | 0.011973302 | Rattus norvegicus F-actin binding protein b-Nexilin mRNA, complete cds. |
| 377134_Rn | 0.011901885 | similar to mouse a disintegrin and metalloprotease with thrombospondin motifs 1 (ADAMTS-1), clone IMAGE:3491991, mRNA, partial cds. |
| AI145097 | 0.011694643 | unknown function |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| BQ782850 | 0.011464648 | similar to Translation of nuc:AL160153_1 Human DNA sequence from clone RP11-397O8 on chromosome 13 Contains the 3 end of the ITBGL1 (integrin, beta-like 1 (with EGF-like repeat domains)) gene, the 3 end of the FGF14 (fibroblast growth factor 14) gene, ESTs, STSs, and GSSs, complete sequence; match: proteins: Tr:O14549 Tr:Q9NPR0 Sw:P09055 Sw:P53712 Sw:P12607 Sw:P07228 Sw:P12606 Sw:P11835 Sw:P49134 Tr:O96444 Tr:O17494. score=7.802e-11 |
| 231197_Rn | 0.011099532 | similar to Mouse DNA sequence from clone RP23-381K21 on chromosome 1, complete sequence. |
| NM_053959 | 0.010933826 | Rattus norvegicus myc box dependent interacting protein 1 (Bin1), mRNA. |
| CB547248 | 0.010900596 | similar to Translation of nuc:BC028939_1 Mus musculus, Similar to PMS1 postmeiotic segregation increased 1 (S. cerevisiae), clone MGC:36491 IMAGE:5364251, mRNA, complete cds. score=2.133e-36 |
| 296334_Rn | 0.010333453 | similar to mouse MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C), clone MGC:25468 IMAGE:4481227, mRNA, complete cds. |
| NM_053522 | 0.01015523 | Rattus norvegicus ras-like protein (Tc10), mRNA. |
| 229083_Rn | 0.009945898 | unknown function |
| 296736_Rn | 0.00993046 | similar to unnamed protein product |
| 216023_Rn | 0.009809025 | Rat hypertrophied skeletal muscle protein FHL1c mRNA, complete cds. |
| 218958_Rn | 0.00966848 | similar to Mouse chromosome 6 clone rp23-176m22 strain C57BL/6J, complete sequence. |
| 207673_Rn | 0.009644362 | similar to Mouse, clone MGC:7583 IMAGE:3493553, mRNA, complete cds. |
| L34821.1 | 0.0095308 | Rat succinate-semialdehyde dehydrogenase (SSADH) mRNA, 3 end. |
| CB547577 | 0.009434145 | similar to Translation of nuc:AF026204_8 Caenorhabditis elegans cosmid C30E1. score=6.062e-09 |
| 298704_Rn | 0.009261067 | similar to TSP2=thrombospondin 2 [Mouse, Genomic, 2030 nt, segment 2 of 2]. |
| 298372_Rn | 0.009118459 | Rat angiotensin II type 1A receptor associated protein mRNA, complete cds. |
| NM_019177 | 0.009110869 | Rattus norvegicus selectin, lymphocyte (Sell), mRNA. |
| CB545139 | 0.008801184 | similar to Translation of nuc:S57132_1 COL16A1=type XVI collagen alpha 1 chain [human, placenta, mRNA Partial, 3720 nt]; This sequence comes from Fig. 2; alpha 1 (XVI). score=2.978e-26 |
| 218107_Rn | 0.008712971 | Rat ASM15 gene. |
| 218836_Rn | 0.008475641 | norvegicus similar to DKFZP586C1619 protein [Homo sapiens] (LOC314675), mRNA. |
| CB547020 | 0.008317261 | similar to GCGPROT:Q64220 THYROTROPIN RECEPTOR (FRAGMENT). score=3.134e-23 |
| CB545955 | 0.008303068 | similar to Protein:NP_598743 expressed sequence AI851155 [Mus musculus]. score=1.798e-52 |
| 259991_Rn | 0.008228418 | similar to Translation of nuc:AK009491_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310024D23, full insert sequence; putative. score=4.186e-39 |
| X89963.1 | 0.008084703 | R.norvegicus mRNA TSP-4 protein. |
| AW144778 | 0.007854843 | unknown function |
| NM_019208 | 0.007826723 | Rattus norvegicus multiple endocrine neoplasia 1 (Men1), mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 219406_Rn | 0.007688372 | similar to mouse CLST 11240 protein, clone MGC:11725 IMAGE:3967350, mRNA, complete cds. |
| AI170794 | 0.007664342 | unknown function |
| CB547931 | 0.007544952 | unknown function |
| 265390_Rn | 0.007506835 | similar to Mouse DNA sequence from clone RP23-132M9 on chromosome X, complete sequence. |
| 222840_Rn | 0.006799741 | Rat mRNA for band83, complete cds. |
| 287902_Rn | 0.006780544 | similar to Mouse, asporin, clone MGC:41375 IMAGE:1365428, mRNA, complete cds. |
| 230838_Rn | 0.006544266 | similar to unnamed protein product |
| BF398773 | 0.006497757 | unknown function |
| CB544919 | 0.006493518 | similar to Protein:NP_060587 WD40 repeat domain 11 protein; WD repeat domain 15 [Homo sapiens]. score=8.275e-65 |
| 295324_Rn | 0.006476527 | similar to Mouse ankyrin repeat-containing SOCS box protein 5 (Asb5) mRNA, complete cds. |
| 208497_Rn | 0.00643506 | similar to Translation of nuc:AF035526_1 Mus musculus kanadaptin mRNA, complete cds. score=6.115e-20 |
| CB606361 | 0.006152612 | similar to Translation of nuc:AK027583_1 Homo sapiens cDNA FLJ14677 fis, clone NT2RP2004095; unnamed protein product. score=6.259e-177 |
| 296678_Rn | 0.005926665 | Rat MS1 mRNA, complete cds. |
| 208020_Rn | 0.005876574 | unknown function |
| CB546554 | 0.00552919 | unknown function |
| 203945_Rn | 0.005471138 | similar to Mouse, clone IMAGE:3598145, mRNA, partial cds. |
| 347349_Rn | 0.005333745 | similar to Mouse early quiescence protein-1 mRNA, complete cds. |
| BI291651 | 0.004985429 | unknown function |
| 296737_Rn | 0.004435824 | similar to Mouse histidine-rich Ca2+ binding protein mRNA, complete cds. |
| 200268_Rn | 0.004369805 | Rattus norvegicus Clusterin (Clu), mRNA. |
| 230761_Rn | 0.004313925 | similar to Translation of nuc:AX055831_1 Sequence 3 from Patent WO0073459; unnamed protein product. score=5.006e-65 |
| 296860_Rn | 0.004274834 | Rattus norvegicus small muscle protein, X-linked (Smpx), mRNA. |
| 298840_Rn | 0.00395162 | Rattus norvegicus connective tissue growth factor (Ctgf), mRNA. |
| AW915945 | 0.003930409 | unknown function |
| 297051_Rn | 0.003823021 | Rattus norvegicus cholinergic receptor, nicotinic, delta polypeptide (Chrnd), mRNA. |
| AA819234 | 0.003735561 | unknown function |
| CB546661 | 0.003727216 | similar to Translation of nuc:AB037835_1 Homo sapiens mRNA for KIAA1414 protein, partial cds; Start codon is not identified. fh14368 cDNA clone for KIAA1414 has a 1-bp insertion at the position 1878 and a 152-bp deletion at the position between 4092 and 4245 of the sequence of KIAA1414.. score=4.604e-37 |
| BF417300 | 0.003664897 | unknown function |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| CB547992 | 0.003377652 | similar to Protein:NP_082427 RIKEN cDNA 2610528A15 [Mus musculus]. score=3.596e-45 |
| 296414_Rn | 0.003353914 | unknown function |
| NM_012786 | 0.003310131 | Rattus norvegicus Cytochrom c oxidase subunit VIII-H (heart/muscle) (Cox8h), mRNA. |
| NM_021588 | 0.003286342 | Rattus norvegicus myoglobin (Mb), mRNA. |
| 295880_Rn | 0.003014336 | UI-R-A0-ad-e-10-0-UI.s1 UI-R-A0 Rattus norvegicus cDNA clone UI-R-A0-ad-e-10-0-UI 3 similar to gb\|N62943\|N62943 yy68h09.s1 Homo sapiens cDNA clone 278753 3, mRNA sequence. |
| 348034_Rn | 0.002724736 | Rattus norvegicus desmin (Des), mRNA. |
| 207121_Rn | 0.002705551 | similar to Protein:NP_081115 RIKEN cDNA 1110055E19 [Mus musculus]. score=2.285e-08 |
| 296824_Rn | 0.002508676 | unknown function |
| 221693_Rn | 0.002503854 | similar to mouse TLH29 protein precursor, clone MGC:25891 IMAGE:4217067, mRNA, complete cds. |
| CB546467 | 0.00244741 | similar to Translation of nuc:BC021222_1 Homo sapiens, clone MGC:12933 IMAGE:4308662, mRNA, complete cds. score=7.92e-55 |
| AF420214.1 | 0.002401046 | Rattus norvegicus tumor necrosis factor receptor type II mRNA, partial cds. |
| 348232_Rn | 0.002400362 | Rattus norvegicus tenomodulin (Tnmd), mRNA. |
| 295561_Rn | 0.002366005 | unknown function |
| CB544878 | 0.002258728 | unknown function |
| BF564613 | 0.002120915 | similar to Protein:NP_542439 Bmp2-inducible kinase [Mus musculus]. score=1.561e-142 |
| NM_017149 | 0.002093591 | Rattus norvegicus mesenchyme homeo box 2 (Meox2), mRNA. |
| NM_080698 | 0.001854949 | Rattus norvegicus fibromodulin (Fmod), mRNA. |
| 229255_Rn | 0.001812349 | similar to Mouse, clone IMAGE:4988852, mRNA, partial cds. |
| 202946_Rn | 0.001802405 | similar to Mouse, RIKEN cDNA 1110018M03 gene, clone MGC:29048 IMAGE:3603588, mRNA, complete cds. |
| 293007_Rn | 0.001780344 | Rattus norvegicus serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1 (Serpine1), mRNA. |
| 291388_Rn | 0.001588115 | Rattus norvegicus cartilage link protein 1 (Crtl1), mRNA. |
| NM_021763 | 0.001552436 | Rattus norvegicus arfaptin 1 (LOC60382), mRNA. |
| J04628.1 | 0.001524132 | GCGNUC:J04628.1; Rattus norvegicus 3-hydroxyiso- butyrate mRNA, 3 end. |
| NM_138900 | 0.001494911 | Rattus norvegicus complement component 1, s subcomponent (C1s), mRNA. |
| 413271_Rn | 0.001423915 | similar to Mouse, secreted modular calcium binding protein 2, clone MGC:28521 IMAGE:4191849, mRNA, complete cds. |
| NM_013104 | 0.001375015 | Rattus norvegicus Insulin-like growth factor binding protein 6 (Igfbp6), mRNA. |
| AW142985 | 0.00125441 | unknown function |
| 430014_Rn | 0.001182215 | Rat troponin-c mRNA. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 206212_Rn | 0.001159988 | Rattus norvegicus actinin alpha 2 associated LIM protein (Pdlim3), mRNA. |
| 202503_Rn | 0.001151385 | Rattus norvegicus histone deacetylase 2 (Hdac2) mRNA, partial cds. |
| 220427_Rn | 0.001019677 | similar to Mouse, clone IMAGE:3991175, mRNA, partial cds. |
| 201221_Rn | 9.85E-04 | unknown function |
| AA818120 | 8.96E-04 | unknown function |
| 220847_Rn | 7.93E-04 | Rattus norvegicus C4 complement protein mRNA, partial cds. |
| AA957467 | 7.87E-04 | similar to Translation of nuc:AK003750_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110017I16, full insert sequence; putative. score=2.217e-25 |
| CB547949 | 7.52E-04 | similar to Protein:NP_573478 myotubularin related protein 4; FYVE zinc finger phosphatase [Mus musculus]. score=7.888e-93 |
| 299009_Rn | 7.46E-04 | similar to Mouse carboxypeptidase X2 mRNA, complete cds. |
| 258706_Rn | 7.15E-04 | unknown function |
| CB546345 | 6.98E-04 | similar to Protein:NP_033996 cadherin 11; OB-cadherin; osteoblast-cadherin [Mus musculus]. score=3.453e-09 |
| 282820_Rn | 6.92E-04 | unknown function |
| BF415205 | 5.51E-04 | Rat mRNA fragment for cardiac actin. |
| BM388714 | 5.33E-04 | unknown function |
| BF523437 | 5.22E-04 | unknown function |
| CB546505 | 5.15E-04 | similar to Protein:NP_033010 protein tyrosine phosphatase, receptor-type, M [Mus musculus]. score=1.044e-80 |
| 222627_Rn | 5.02E-04 | Rattus norvegicus Troponin I, slow isoform (Tnni1), mRNA. |
| 217038_Rn | 4.92E-04 | Rattus norvegicus Insulin-like growth factor II (somatomedin A) (Igf2), mRNA. |
| NM_057191 | 4.58E-04 | Rattus norvegicus sarcomeric muscle protein (Sarcosin), mRNA. |
| 207465_Rn | 4.56E-04 | similar to Translation of nuc:AK003938_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110027O12, full insert sequence; putative. score=7.721e-11 |
| 232141_Rn | 3.45E-04 | similar to cartilage intermediate layer protein |
| 201251_Rn | 3.22E-04 | similar to Mouse putative potassium-chloride cotransporter-4 (Kcc4) mRNA, complete cds. |
| 200736_Rn | 2.01E-04 | Rattus norvegicus myosin heavy chain, polypeptide 6, cardiac muscle, alpha (Myh6), mRNA. |
| AI579422 | 1.58E-04 | unknown function |
| NM_013220 | 1.52E-04 | Rattus norvegicus ankyrin-like repeat protein (Alrp), mRNA. |
| 295023_Rn | 1.43E-04 | similar to Translation of nuc:AK003750_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110017I16, full insert sequence; putative. score=2.217e-25 |
| AI409191 | 1.35E-04 | unknown function |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 347198_Rn | 1.33E-04 | similar to Mouse, RIKEN cDNA 2310045A07 gene, clone MGC:41044 IMAGE:1397989, mRNA, complete cds. |
| 229336_Rn | 1.20E-04 | similar to Mouse collagenous repeat-containing sequence of 26kDa protein (CORS26) mRNA, complete cds. |
| NM_030868 | 7.75E-05 | Rattus norvegicus NOV protein (Nov), mRNA. |
| 327164_Rn | 6.21E-05 | similar to Mouse REX-3 mRNA, complete cds. |
| 199437_Rn | 5.94E-05 | Rattus norvegicus Neuron specific protein PEP-19 (Purkinje cell protein 4) (Pcp4), mRNA. |
| 217522_Rn | 5.67E-05 | Rattus norvegicus actinin alpha 3 (Actn3), mRNA. |
| NM_057144 | 4.43E-05 | Rattus norvegicus cysteine-rich protein 3 (Csrp3), mRNA. |
| NM_022499 | 1.02E-05 | Rattus norvegicus Parvalbumin (calcium binding protein) (Pvalb), mRNA. |
| 284707_Rn | 8.63E-06 | Rattus norvegicus chondromodulin-1 (Chm-1), mRNA. |
| NM_012929 | 5.35E-07 | Rattus norvegicus Procollagen II alpha 1 (Col2a1), mRNA. |
| BF560915 | 4.85E-07 | Rattus norvegicus mRNA for collagen alpha 1 type X, partial. |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold DOWN-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 297538_Rn | 0.04702519 | similar to Mouse mRNA for Ky protein (muscle-specific protein). |
| NM_012589 | 0.046647282 | Rattus norvegicus Interleukin 6 (interferon, beta 2) (Il6), mRNA. |
| 296913_Rn | 0.04407278 | similar to Mouse myocytic induction/differentiation originator mRNA, complete cds. |
| BE115700 | 0.04088808 | unknown function |
| AW918099 | 0.036855822 | unknown function |
| 217925_Rn | 0.036667956 | similar to Mouse mRNA for M-protein. |
| 292212_Rn | 0.033939721 | Rattus norvegicus Small inducible gene JE (Scya2), mRNA. |
| BQ781375 | 0.033572781 | similar to Protein:NP_067483 myozenin; skeletal muscle-specific protein; calcineurin-2 [Mus musculus]. score=7.91e-40 |
| 219978_Rn | 0.033154467 | Rat mRNA for glycerol 3-phosphate dehydrogenase, complete cds. |
| 218360_Rn | 0.026208044 | similar to Mouse, integrin beta 1 binding protein 2, clone MGC:41122 IMAGE:1346742, mRNA, complete cds. |
| AF059344.1 | 0.020868903 | Rattus norvegicus titin mRNA, partial cds. |
| NM_022177 | 0.017225533 | Rattus norvegicus Stromal cell-derived factor 1 (Sdf1), mRNA. |
| NM_017328 | 0.016465715 | Rattus norvegicus phosphoglycerate mutase 2 (Pgam2), mRNA. |
| NM_017066 | 0.016209628 | Rattus norvegicus Pleiotrophin (Heparine binding factor, Hbnf, in the mouse) (Ptn), mRNA. |
| 220752_Rn | 0.014938742 | Rattus norvegicus sodium channel, voltage-gated, type I, beta polypeptide (Scn1b), mRNA. |
| 297410_Rn | 0.013684151 | Rattus norvegicus ryanodine receptor type 1 (RyR1) mRNA, partial cds. |
| 204921_Rn | 0.013543894 | similar to Translation of nuc:AY036877_1 Mus musculus actinin alpha 2 (Actn2) mRNA, complete cds. score=6.755e-91 |
| AA900269 | 0.011681645 | similar to gi\|1304380\|gb\|U29528\|RNU29528 Rattus norvegicus hemoglobin alpha chain gene, complete cds, mRNA sequence. |
| 205248_Rn | 0.01159689 | similar to sarcoplasmic reticulum glycoprotein |
| 204961_Rn | 0.009391028 | similar to unnamed protein product |
| BF550734 | 0.009282715 | unknown function |
| 226731_Rn | 0.008615446 | similar to Translation of nuc:AK009352_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310015C21, full insert sequence; putative. score=1.161e-42 |
| 326761_Rn | 0.007156469 | similar to Mouse RING-finger protein MURF mRNA, complete cds. |
| 220641_Rn | 0.006185176 | similar to data source:SPTR, source key:Q99969, evidence:ISS~homolog to RETINOIC ACID RECEPTOR RESPONDER PROTEIN 2 PRECURSOR (TAZAROTENE- INDUCED GENE 2 PROTEIN) (RAR-RESPONSIVE PROTEIN TIG2)~putative |
| 222395_Rn | 0.006176233 | Rat mRNA for sarcomeric mitochondrial creatine kinase. |
| BQ194536 | 0.006085215 | similar to Protein:NP_033824 apolipoprotein B editing complex 2 [Mus musculus]. score=7.281e-97 |

**Table 2: Significant 2-Fold Gene Expression Changes at 11 Days Fracture Healing**
**Greater than 2-Fold DOWN-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 220080_Rn | 0.005352806 | similar to Protein:NP_067483 myozenin; skeletal muscle-specific protein; calcineurin-2 [Mus musculus]. score=4.677e-48 |
| 200403_Rn | 0.003595361 | Rat mRNA for atrial myosin light chain 1. |
| 218799_Rn | 0.003300111 | similar to Mouse mRNA for stretch responsive protein (gene Tims). |
| 200849_Rn | 0.00273697 | Rattus norvegicus Creatine kinase, muscle form (Ckm), mRNA. |
| 296247_Rn | 0.002724828 | similar to Mouse cypher1 mRNA, complete cds. |
| 280399_Rn | 0.002007331 | similar to mouse Ig joining chain, clone MGC:6626 IMAGE:3491646, mRNA, complete cds. |
| 216910_Rn | 0.001884423 | similar to Protein:NP_033824 apolipoprotein B editing complex 2 [Mus musculus]. score=7.281e-97 |
| BF285291 | 0.001606058 | unknown function |
| NM_031813 | 4.80E-04 | Rattus norvegicus norvegicus myosin binding protein H (Mybph), mRNA. |
| CB548063 | 2.82E-04 | similar to Translation of nuc:BC022248_1 Homo sapiens, Similar to DnaJ (Hsp40) homolog, subfamily B, member 12, clone MGC:22187 IMAGE:4771526, mRNA, complete cds. score=2.211e-56 |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 293162_Rn | 0.049065665 | similar to hypothetical protein FLJ13236 |
| 344269_Rn | 0.049065665 | Rattus norvegicus sodium-coupled citrate transporter (NaCT), mRNA. |
| BQ204885 | 0.047362652 | unknown function |
| NM_019289 | 0.047362652 | Rattus norvegicus Actin-related protein complex 1b (Arpc1b), mRNA. |
| 296678_Rn | 0.047315244 | Rat MS1 mRNA, complete cds. |
| BQ208015 | 0.046880281 | similar to Protein:NP_081121 peptidylprolyl isomerase (cyclophilin)-like 1 [Mus musculus]. score=9.871e-82 |
| 230838_Rn | 0.046366731 | similar to unnamed protein product |
| CB547489 | 0.04572215 | similar to Translation of nuc:AB067489_1 Homo sapiens mRNA for KIAA1902 protein, partial cds; Start codon is not identified.. score=3.858e-51 |
| 222395_Rn | 0.045331181 | Rat mRNA for sarcomeric mitochondrial creatine kinase. |
| CB544919 | 0.045211033 | similar to Protein:NP_060587 WD40 repeat domain 11 protein; WD repeat domain 15 [Homo sapiens]. score=8.275e-65 |
| 203358_Rn | 0.045211033 | Rat c-fos mRNA. |
| CB546554 | 0.045200028 | unknown function |
| 217893_Rn | 0.045200028 | Rattus norvegicus heat shock 70kD protein 5 (Hspa5), mRNA. |
| 222534_Rn | 0.045072793 | similar to Mouse, clone IMAGE:3583970, mRNA, partial cds. |
| BF398773 | 0.043516823 | unknown function |
| 218904_Rn | 0.043516823 | similar to KIAA0782 protein |
| AA858954 | 0.043073552 | unknown function |
| 221755_Rn | 0.043073552 | unknown function |
| 203945_Rn | 0.042985576 | similar to Mouse, clone IMAGE:3598145, mRNA, partial cds. |
| 208250_Rn | 0.042497156 | Rattus norvegicus interferon gamma receptor (Ifngr), mRNA. |
| 219309_Rn | 0.042231739 | Rat heme oxygenase gene, complete cds. |
| AA819234 | 0.041928152 | unknown function |
| BE107038 | 0.041928152 | unknown function |
| 217925_Rn | 0.041287368 | similar to Mouse mRNA for M-protein. |
| NM_012587 | 0.041287368 | Rattus norvegicus integrin binding sialoprotein (Ibsp), mRNA. |
| 287902_Rn | 0.040389711 | similar to Mouse, asporin, clone MGC:41375 IMAGE:1365428, mRNA, complete cds. |
| 298983_Rn | 0.039487435 | similar to myopalladin |
| 219058_Rn | 0.039020125 | Rattus norvegicus S100 calcium-binding protein A9 (calgranulin B) (S100a9), mRNA. |
| 226731_Rn | 0.038435721 | similar to Translation of nuc:AK009352_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310015C21, full insert sequence; putative. score=1.161e-42 |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 205248_Rn | 0.037833766 | similar to sarcoplasmic reticulum glycoprotein |
| U57362.1 | 0.037810091 | Rattus norvegicus collagen XII alpha 1 (Col12a1) mRNA, partial cds. |
| 203776_Rn | 0.037459117 | Rattus norvegicus glycoprotein (transmembrane) nmb (Gpnmb), mRNA. |
| 220641_Rn | 0.035760314 | similar to data source:SPTR, source key:Q99969, evidence:ISS~homolog to RETINOIC ACID RECEPTOR RESPONDER PROTEIN 2 PRECURSOR (TAZAROTENE- INDUCED GENE 2 PROTEIN) (RAR-RESPONSIVE PROTEIN TIG2)~putative |
| AI411057 | 0.034915752 | unknown function |
| NM_012786 | 0.034177803 | Rattus norvegicus Cytochrom c oxidase subunit VIII-H (heart/muscle) (Cox8h), mRNA. |
| 298840_Rn | 0.034177803 | Rattus norvegicus connective tissue growth factor (Ctgf), mRNA. |
| 298460_Rn | 0.034081546 | Rattus norvegicus Early growth response 1 (Egr1), mRNA. |
| BQ209028 | 0.033524821 | unknown function |
| 322818_Rn | 0.033524821 | similar to Mouse, clone IMAGE:3489640, mRNA. |
| 215841_Rn | 0.033446149 | similar to Mouse DNA sequence from clone RP23-406B13 on chromosome 4, complete sequence. |
| 202815_Rn | 0.032914575 | similar to Mouse, RIKEN cDNA 1300011C24 gene, clone MGC:7169 IMAGE:3257323, mRNA, complete cds. |
| BF417300 | 0.032885657 | unknown function |
| BF558699 | 0.032580888 | unknown function |
| 200268_Rn | 0.032237305 | Rattus norvegicus Clusterin (Clu), mRNA. |
| 221395_Rn | 0.030997999 | similar to Protein:NP_080731 RIKEN cDNA 2510049I19 gene [Mus musculus]. score=5.034e-32 |
| CB606361 | 0.030997999 | similar to Translation of nuc:AK027583_1 Homo sapiens cDNA FLJ14677 fis, clone NT2RP2004095; unnamed protein product. score=6.259e-177 |
| 222867_Rn | 0.030997999 | Rattus norvegicus Benzodiazepin receptor (peripheral) (Bzrp), mRNA. |
| 206584_Rn | 0.030997999 | Rattus norvegicus smooth muscle cell LIM protein (SmLIM) mRNA, complete cds. |
| BI291651 | 0.029780122 | unknown function |
| BQ189985 | 0.029774468 | Rattus norvegicus high-affinity immunoglobulin gamma Fc receptor I mRNA, partial cds. |
| NM_017148 | 0.029727025 | Rattus norvegicus cysteine rich protein 1 (Csrp1), mRNA. |
| 204921_Rn | 0.028954673 | similar to Translation of nuc:AY036877_1 Mus musculus actinin alpha 2 (Actn2) mRNA, complete cds. score=6.755e-91 |
| NM_013091 | 0.028352338 | Rattus norvegicus Tumor necrosis factor receptor (Tnfr1), mRNA. |
| 295880_Rn | 0.028352338 | UI-R-A0-ad-e-10-0-UI.s1 UI-R-A0 Rattus norvegicus cDNA clone UI-R-A0-ad-e-10-0-UI 3 similar to gb\|N62943\|N62943 yy68h09.s1 Homo sapiens cDNA clone 278753 3, mRNA sequence. |
| AW918099 | 0.028352338 | unknown function |
| NM_017328 | 0.027215663 | Rattus norvegicus phosphoglycerate mutase 2 (Pgam2), mRNA. |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| CB546661 | 0.026862147 | similar to Translation of nuc:AB037835_1 Homo sapiens mRNA for KIAA1414 protein, partial cds; Start codon is not identified. fh14368 cDNA clone for KIAA1414 has a 1-bp insertion at the position 1878 and a 152-bp deletion at the position between 4092 and 4245 of the sequence of KIAA1414.. score=4.604e-37 |
| 218553_Rn | 0.026697054 | similar to Protein:NP_031447 adenylosuccinate synthetase 1, muscle [Mus musculus]. score=5.795e-85 |
| AW915945 | 0.026697054 | unknown function |
| 348034_Rn | 0.026693981 | Rattus norvegicus desmin (Des), mRNA. |
| 413406_Rn | 0.026693981 | UI-R-A1-eo-f-12-0-UI.s1 UI-R-A1 Rattus norvegicus cDNA clone UI-R-A1-eo-f-12-0-UI 3 similar to gi\|2918669\|dbj\|C86712\|C86712 Mus musculus fertilized egg cDNA 3-end sequence, clone J0231G01, mRNA sequence. |
| 200661_Rn | 0.026625164 | similar to Mouse, clone MGC:6469 IMAGE:2631779, mRNA, complete cds. |
| NM_134334 | 0.025034746 | Rattus norvegicus cathepsin D (Ctsd), mRNA. |
| U75926.1 | 0.025034746 | Rattus norvegicus cytochrome oxidase subunit VIIa mRNA, 5 untranslated region, partial sequence. |
| 292212_Rn | 0.024852451 | Rattus norvegicus Small inducible gene JE (Scya2), mRNA. |
| 347349_Rn | 0.023998962 | similar to Mouse early quiescence protein-1 mRNA, complete cds. |
| 201560_Rn | 0.022807921 | similar to Translation of nuc:AK002214_1 Mus musculus adult male kidney cDNA, RIKEN full-length enriched library, clone:0610005A19, full insert sequence; putative. score=1.142e-28 |
| AA858962 | 0.022807921 | Rat retinol-binding protein (RBP) mRNA, partial cds. |
| BQ200384 | 0.022807921 | unknown function |
| CB547992 | 0.022807921 | similar to Protein:NP_082427 RIKEN cDNA 2610528A15 [Mus musculus]. score=3.596e-45 |
| CA509950 | 0.022323819 | Rattus sp. 3 UTR. |
| NM_022510 | 0.022323819 | Rattus norvegicus ribosomal protein L4 (Rpl4), mRNA. |
| 199948_Rn | 0.022323819 | Rattus norvegicus Farnesyl diphosphate synthase (Fdps), mRNA. |
| 222544_Rn | 0.022211891 | Rattus norvegicus Cholesterol esterase (pancreatic) (Lipa), mRNA. |
| BQ210920 | 0.021803968 | unknown function |
| BE105985 | 0.021492965 | unknown function |
| 222629_Rn | 0.019689063 | Rattus norvegicus embigin (Emb), mRNA. |
| AA858647 | 0.019409652 | unknown function |
| NM_017149 | 0.019112443 | Rattus norvegicus mesenchyme homeo box 2 (Meox2), mRNA. |
| 221213_Rn | 0.019112443 | Rattus norvegicus Syndecan 1 (Sdc1), mRNA. |
| 204961_Rn | 0.017996057 | similar to unnamed protein product |
| AW525201 | 0.017996057 | unknown function |
| 296737_Rn | 0.017442419 | similar to Mouse histidine-rich Ca2+ binding protein mRNA, complete cds. |
| 297051_Rn | 0.016703667 | Rattus norvegicus cholinergic receptor, nicotinic, delta polypeptide (Chrnd), mRNA. |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 230761_Rn | 0.016479583 | similar to Translation of nuc:AX055831_1 Sequence 3 from Patent WO0073459; unnamed protein product. score=5.006e-65 |
| NM_013026 | 0.016103594 | Rattus norvegicus Syndecan (Synd1), mRNA. |
| 201953_Rn | 0.01598859 | similar to Mouse EIA (Serpinb1) mRNA, complete cds. |
| 206738_Rn | 0.01598859 | Rat metallothionein-2 and metallothionein-1 genes, complete cds. |
| 295561_Rn | 0.015844812 | unknown function |
| NM_080698 | 0.015681369 | Rattus norvegicus fibromodulin (Fmod), mRNA. |
| 207121_Rn | 0.014645637 | similar to Protein:NP_081115 RIKEN cDNA 1110055E19 [Mus musculus]. score=2.285e-08 |
| CB545131 | 0.014645637 | similar to Protein:NP_055392 bromodomain containing protein 1; BR140-like gene [Homo sapiens]. score=7.563e-63 |
| BQ194536 | 0.014645637 | similar to Protein:NP_033824 apolipoprotein B editing complex 2 [Mus musculus]. score=7.281e-97 |
| 219818_Rn | 0.014447432 | similar to Mouse spermidine/spermine N1-acetyltransferase (SSAT) mRNA, complete cds. |
| AA859114 | 0.014447432 | similar to Protein:NP_080712 RIKEN cDNA 1810054O13 [Mus musculus]. score=6.377e-40 |
| CB546467 | 0.014338782 | similar to Translation of nuc:BC021222_1 Homo sapiens, clone MGC:12933 IMAGE:4308662, mRNA, complete cds. score=7.92e-55 |
| AF420214.1 | 0.014338782 | Rattus norvegicus tumor necrosis factor receptor type II mRNA, partial cds. |
| 221693_Rn | 0.014318903 | similar to mouse TLH29 protein precursor, clone MGC:25891 IMAGE:4217067, mRNA, complete cds. |
| 202946_Rn | 0.013828435 | similar to Mouse, RIKEN cDNA 1110018M03 gene, clone MGC:29048 IMAGE:3603588, mRNA, complete cds. |
| 295729_Rn | 0.013579155 | Rat thymocyte L-CA (leukocyte common antigen) mRNA, 3 flank. |
| 220080_Rn | 0.0133583 | similar to Protein:NP_067483 myozenin; skeletal muscle-specific protein; calcineurin-2 [Mus musculus]. score=4.677e-48 |
| 199927_Rn | 0.012716027 | Rattus norvegicus H3 histone, family 3B (H3f3b), mRNA. |
| 296824_Rn | 0.012547921 | unknown function |
| NM_021588 | 0.012547921 | Rattus norvegicus myoglobin (Mb), mRNA. |
| 296860_Rn | 0.012538196 | Rattus norvegicus small muscle protein, X-linked (Smpx), mRNA. |
| 200663_Rn | 0.012538196 | Rattus norvegicus vimentin (Vim), mRNA. |
| BF564613 | 0.012538196 | similar to Protein:NP_542439 Bmp2-inducible kinase [Mus musculus]. score=1.561e-142 |
| 229255_Rn | 0.012538196 | similar to Mouse, clone IMAGE:4988852, mRNA, partial cds. |
| NM_138900 | 0.012538196 | Rattus norvegicus complement component 1, s subcomponent (C1s), mRNA. |
| 231072_Rn | 0.012538196 | similar to Mouse, clone IMAGE:3589736, mRNA, partial cds. |
| 292104_Rn | 0.012277109 | similar to Translation of nuc:BC032959_1 Mus musculus, triggering receptor expressed on myeloid cells 2a, clone MGC:40999 IMAGE:1348066, mRNA, complete cds. score=2.498e-69 |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 200403_Rn | 0.012277109 | Rat mRNA for atrial myosin light chain 1. |
| 221153_Rn | 0.011881815 | Rattus norvegicus mRNA for cathepsin Y, partial cds. |
| CB548315 | 0.011881815 | similar to Protein:NP_084515 ATP-binding cassette, subfamily G, member 3 [Mus musculus]. score=6.816e-62 |
| 385033_Rn | 0.011794992 | Rattus norvegicus high mobility group box 2 (Hmgb2), mRNA. |
| 206075_Rn | 0.011636887 | similar to mouse annexin A8, clone MGC:13875 IMAGE:4013266, mRNA, complete cds. |
| NM_017066 | 0.011403199 | Rattus norvegicus Pleiotrophin (Heparine binding factor, Hbnf, in the mouse) (Ptn), mRNA. |
| 296381_Rn | 0.011403199 | similar to RAB5 interacting protein 3 |
| NM_021763 | 0.011306492 | Rattus norvegicus arfaptin 1 (LOC60382), mRNA. |
| CB547219 | 0.011202141 | unknown function |
| AA900381 | 0.010708936 | unknown function |
| 292230_Rn | 0.010664541 | Rattus norvegicus dual specificity phosphatase 6 (Dusp6), mRNA. |
| NM_031813 | 0.010108819 | Rattus norvegicus norvegicus myosin binding protein H (Mybph), mRNA. |
| NM_138828 | 0.009795748 | Rattus norvegicus Apolipoprotein E, (Apoe), mRNA. |
| 206212_Rn | 0.009795748 | Rattus norvegicus actinin alpha 2 associated LIM protein (Pdlim3), mRNA. |
| BQ781375 | 0.009540745 | similar to Protein:NP_067483 myozenin; skeletal muscle-specific protein; calcineurin-2 [Mus musculus]. score=7.91e-40 |
| NM_017055 | 0.009481938 | Rattus norvegicus Transferrin (Tf), mRNA. |
| 413271_Rn | 0.009251402 | similar to Mouse, secreted modular calcium binding protein 2, clone MGC:28521 IMAGE:4191849, mRNA, complete cds. |
| 273885_Rn | 0.009137271 | Rattus norvegicus complement component 5, receptor 1 (C5r1), mRNA. |
| 298020_Rn | 0.00894185 | similar to Mouse homeobox gene Prx2 mRNA. |
| NM_013156 | 0.00894185 | Rattus norvegicus Cathepsin L (Ctsl), mRNA. |
| 280399_Rn | 0.00851745 | similar to mouse Ig joining chain, clone MGC:6626 IMAGE:3491646, mRNA, complete cds. |
| 202503_Rn | 0.00846734 | Rattus norvegicus histone deacetylase 2 (Hdac2) mRNA, partial cds. |
| NM_013104 | 0.008252958 | Rattus norvegicus Insulin-like growth factor binding protein 6 (Igfbp6), mRNA. |
| AW142985 | 0.008252958 | unknown function |
| J04628.1 | 0.007983283 | GCGNUC:J04628.1; Rattus norvegicus 3-hydroxyiso- butyrate mRNA, 3 end. |
| 217733_Rn | 0.007983283 | similar to Mouse, RIKEN cDNA 1300019I03 gene, clone MGC:6625 IMAGE:3491528, mRNA, complete cds. |
| 208320_Rn | 0.007816396 | similar to evidence:NAS~hypothetical protein~putative |
| 296247_Rn | 0.007816396 | similar to Mouse cypher1 mRNA, complete cds. |
| 348232_Rn | 0.007816396 | Rattus norvegicus tenomodulin (Tnmd), mRNA. |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_053843 | 0.007801117 | Rattus norvegicus Fc receptor, IgG, low affinity III (Fcgr3), mRNA. |
| 223588_Rn | 0.007578489 | Rattus norvegicus macrophage galactose N-acetyl-galactosamine specific lectin (Mgl), mRNA. |
| 294206_Rn | 0.007532748 | similar to Mouse strain C57BL/6J basilin mRNA, complete cds. |
| CB606336 | 0.006914106 | unknown function |
| 343323_Rn | 0.006486278 | similar to Mouse FKBP65 binding protein mRNA, complete cds. |
| 208234_Rn | 0.005333962 | Rattus norvegicus coronin, actin binding protein 1A (Coro1a), mRNA. |
| 216910_Rn | 0.005333962 | similar to Protein:NP_033824 apolipoprotein B editing complex 2 [Mus musculus]. score=7.281e-97 |
| 293007_Rn | 0.005084269 | Rattus norvegicus serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1 (Serpine1), mRNA. |
| 220847_Rn | 0.005084269 | Rattus norvegicus C4 complement protein mRNA, partial cds. |
| 220427_Rn | 0.005084269 | similar to Mouse, clone IMAGE:3991175, mRNA, partial cds. |
| CB544878 | 0.005084269 | unknown function |
| 201221_Rn | 0.004667983 | unknown function |
| 282820_Rn | 0.00436441 | unknown function |
| CB547949 | 0.00436441 | similar to Protein:NP_573478 myotubularin related protein 4; FYVE zinc finger phosphatase [Mus musculus]. score=7.888e-93 |
| BF285291 | 0.00436441 | unknown function |
| 200849_Rn | 0.004166174 | Rattus norvegicus Creatine kinase, muscle form (Ckm), mRNA. |
| CB546345 | 0.004130372 | similar to Protein:NP_033996 cadherin 11; OB-cadherin; osteoblast-cadherin [Mus musculus]. score=3.453e-09 |
| AA818120 | 0.003743649 | unknown function |
| NM_131914 | 0.003731393 | Rattus norvegicus caveolin 2 (Cav2), mRNA. |
| BF415205 | 0.003731393 | Rat mRNA fragment for cardiac actin. |
| NM_057191 | 0.003447402 | Rattus norvegicus sarcomeric muscle protein (Sarcosin), mRNA. |
| BF523437 | 0.003300256 | unknown function |
| 299009_Rn | 0.003300256 | similar to Mouse carboxypeptidase X2 mRNA, complete cds. |
| 296414_Rn | 0.003300256 | unknown function |
| CB546505 | 0.003300256 | similar to Protein:NP_033010 protein tyrosine phosphatase, receptor-type, M [Mus musculus]. score=1.044e-80 |
| 208422_Rn | 0.002529398 | Rattus norvegicus alanyl (membrane) aminopeptidase (Anpep), mRNA. |
| NM_033539 | 0.002032439 | Rattus norvegicus eukaryotic translation elongation factor 1 alpha 2 (Eef1a2), mRNA. |
| BM388714 | 0.0018133 | unknown function |
| AW526982 | 0.001705411 | unknown function |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| CB548041 | 0.001705411 | similar to Protein:NP_663384 similar to cutlet [Mus musculus]. score=1.492e-20 |
| 201251_Rn | 0.001635916 | similar to Mouse putative potassium-chloride cotransporter-4 (Kcc4) mRNA, complete cds. |
| AA957467 | 0.001434298 | similar to Translation of nuc:AK003750_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110017I16, full insert sequence; putative. score=2.217e-25 |
| 222627_Rn | 0.001395462 | Rattus norvegicus Troponin I, slow isoform (Tnni1), mRNA. |
| 412899_Rn | 0.001347668 | similar to Mouse Strain C57BL6/J Chromosome X BAC, RP23-64A09, Complete Sequence, complete sequence. |
| CB548063 | 0.001266003 | similar to Translation of nuc:BC022248_1 Homo sapiens, Similar to DnaJ (Hsp40) homolog, subfamily B, member 12, clone MGC:22187 IMAGE:4771526, mRNA, complete cds. score=2.211e-56 |
| 217038_Rn | 0.001266003 | Rattus norvegicus Insulin-like growth factor II (somatomedin A) (Igf2), mRNA. |
| NM_022226 | 0.001260916 | Rattus norvegicus protease, cysteine, 1 (legumain) (Prsc1), mRNA. |
| 232141_Rn | 0.001260916 | similar to cartilage intermediate layer protein |
| BQ205045 | 8.84E-04 | unknown function |
| NM_012771 | 8.60E-04 | Rattus norvegicus Lysozyme (Lyz), mRNA. |
| 207465_Rn | 8.06E-04 | similar to Translation of nuc:AK003938_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110027O12, full insert sequence; putative. score=7.721e-11 |
| AI579422 | 8.03E-04 | unknown function |
| 215832_Rn | 6.87E-04 | similar to Mouse, RIKEN cDNA 3110037K17 gene, clone MGC:41407 IMAGE:1496162, mRNA, complete cds. |
| NM_013220 | 6.74E-04 | Rattus norvegicus ankyrin-like repeat protein (Alrp), mRNA. |
| 347198_Rn | 4.84E-04 | similar to Mouse, RIKEN cDNA 2310045A07 gene, clone MGC:41044 IMAGE:1397989, mRNA, complete cds. |
| 258706_Rn | 4.84E-04 | unknown function |
| 229336_Rn | 4.84E-04 | similar to Mouse collagenous repeat-containing sequence of 26kDa protein (CORS26) mRNA, complete cds. |
| AI409191 | 4.84E-04 | unknown function |
| 200736_Rn | 4.27E-04 | Rattus norvegicus myosin heavy chain, polypeptide 6, cardiac muscle, alpha (Myh6), mRNA. |
| 291388_Rn | 2.87E-04 | Rattus norvegicus cartilage link protein 1 (Crtl1), mRNA. |
| 327164_Rn | 2.87E-04 | similar to Mouse REX-3 mRNA, complete cds. |
| 295023_Rn | 2.87E-04 | similar to Translation of nuc:AK003750_1 Mus musculus 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110017I16, full insert sequence; putative. score=2.217e-25 |
| NM_030868 | 2.87E-04 | Rattus norvegicus NOV protein (Nov), mRNA. |
| 217522_Rn | 2.87E-04 | Rattus norvegicus actinin alpha 3 (Actn3), mRNA. |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold UP-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_057144 | 2.49E-04 | Rattus norvegicus cysteine-rich protein 3 (Csrp3), mRNA. |
| 199437_Rn | 2.39E-04 | Rattus norvegicus Neuron specific protein PEP-19 (Purkinje cell protein 4) (Pcp4), mRNA. |
| NM_022499 | 2.19E-05 | Rattus norvegicus Parvalbumin (calcium binding protein) (Pvalb), mRNA. |
| 284707_Rn | 5.00E-07 | Rattus norvegicus chondromodulin-1 (Chm-1), mRNA. |
| NM_012929 | 8.32E-08 | Rattus norvegicus Procollagen II alpha 1 (Col2a1), mRNA. |
| BF560915 | 8.32E-08 | Rattus norvegicus mRNA for collagen alpha 1 type X, partial. |

**Table 3: Significant 2-Fold Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**Greater than 2-Fold DOWN-regulated**

| Gene ID | P-value | Gene Function |
|---|---|---|
| 200837_Rn | 0.031732148 | Rattus norvegicus defensin NP-2 precursor (LOC286995), mRNA. |

**Table 3: Significant Gene Expression Changes Between 3 Days and 11 Days Fracture Healing**
**UP or DOWN-regulated LESS than 2-Fold**

| Gene ID | P-value | Gene Function |
|---|---|---|
| NM_019289 | 0.047362652 | Rattus norvegicus Actin-related protein complex 1b (Arpc1b), mRNA. |
| 230838_Rn | 0.046366731 | similar to unnamed protein product, AI105049 |
| 222395_Rn | 0.045331181 | Rat mRNA for sarcomeric mitochondrial creatine kinase. |
| BF398773 | 0.043516823 | unknown function |
| AA858954 | 0.043073552 | unknown function |
| 203945_Rn | 0.042985576 | similar to Mouse, clone IMAGE:3598145, mRNA, partial cds. |
| 219309_Rn | 0.042231739 | Rat heme oxygenase gene, complete cds. |
| 226731_Rn | 0.038435721 | similar to Translation of nuc:AK009352_1 Mus musculus adult male tongue cDNA, RIKEN full-length enriched library, clone:2310015C21, full insert sequence; putative. score=1.161e-42 |
| 203776_Rn | 0.037459117 | Rattus norvegicus glycoprotein (transmembrane) nmb (Gpnmb), mRNA. |
| 220641_Rn | 0.035760314 | similar to data source:SPTR, source key:Q99969, evidence:ISS~homolog to RETINOIC ACID RECEPTOR RESPONDER PROTEIN 2 PRECURSOR (TAZAROTENE- INDUCED GENE 2 PROTEIN) (RAR-RESPONSIVE PROTEIN TIG2)~putative |
| AI411057 | 0.034915752 | unknown function |
| BF558699 | 0.032580888 | Cytochrome b-245 light chain, Critical component of the membrane-bound oxidase of phagocytes that generates superoxide |
| 385033_Rn | 0.011794992 | Rattus norvegicus high mobility group box 2 (Hmgb2), mRNA. |
| NM_017055 | 0.009481938 | Rattus norvegicus Transferrin (Tf), mRNA. |